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L5 ANSWER 1 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
2006:13021 Document No. 144:101055 Protein Sp35/LINGO-1 antagonists for treatment of conditions involving demyelination. Mi, Sha; Pepinsky, R. Blake; McCoy, John (Biogen Idec Ma Inc., USA). PCT Int. Appl. WO 2006002437 A2 20060105, 183 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-US22881 20050624. PRIORITY: US 2004-2004/PV58296U 20040624; US 2004-2004/PV61729U 20041007; US 2004-2004/PV62843U 20041115; US 2005-2005/PV680475 20050513.
AB The invention provides methods of treating diseases, disorders or injuries involving demyelination and dysmyelination, including multiple sclerosis, by the administration of an Sp35/LINGO-1 antagonist. The Sp35/LINGO-1 antagonists include soluble Sp35 peptides, Sp35 **fusion** products

with antibodies or antibody fragments, and Sp35 antisense polynucleotides, ribozymes, siRNA, or small hairpin RNA. The invention further claims polypeptide sequences for human Sp35 polypeptide and peptides, and a DNA sequence for an Sp35 shRNA. The human Sp35 protein contains signal sequence, a domain with 14 leucine-rich repeats, an Ig domain, a transmembrane region, and a cytoplasmic domain. The human Sp35 gene contains alternative translation start codons, so that 6 addnl. amino acids may or may not be present at the N-terminus of the Sp35 signal sequence. Rat oligodendrocyte precursor cells were infected with a lentiviral vector containing Sp35/LINGO-1 RNAi. Endogenous Sp35 expression was reduced as determined by RT-PCR and this resulted in more highly differentiated, mature oligodendrocytes compared with the control. An Sp35-**Fc fusion** protein was constructed using the extracellular region of human Sp35 and human IgG1 **Fc** region. Purified recombinant Sp35-**Fc** protein promoted differentiation of rat precursor cells into O4-expressing mature oligodendrocytes and increased the in vitro survival rate for **MBP**-expressing mature oligodendrocytes. Sp35-**Fc fusion** protein and Ig domain peptides of Sp35 promoted myelination in vitro in co-cultures of rat dorsal root ganglion neurons and oligodendrocytes. In vivo transplantation of Sp35-transformed cells to injured rat spinal cords resulted in more oligodendrocyte and axon myelination and less axon retraction than in the control.

L5 ANSWER 2 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

2006:12955 Document No. 144:126919 Genes showing altered levels of expression in melanoma, nevi, and skin and their use in the rapid identification of malignant melanocytes. Wang, Yixin; Talantov, Dimitri; Mazumder, Abhijit (Veridex, LLC, USA). PCT Int. Appl. WO 2006002433 A2 20060105, 435 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-US22846 20050624. PRIORITY: US 2004-2004/PV582906 20040625.

AB Genes that show different levels of expression in melanoma cells or nevi in comparison to normal skin are identified. These genes can be used as markers to diagnose melanoma and can identify micrometastases. The assay can be performed on lymph node tissue. Identification of a small number of highly informative genes in a com. microarray is reported.

L5 ANSWER 3 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

2005:1200359 Document No. 143:458504 CD40 variants, muteins, polynucleotides, **fusion** molecules and antibodies for diagnosis, prevention and treatment of cancer, inflammation, ischemia, infection, autoimmune and immune disease. Marshall, Shannon A.; Linnemann, Thomas; Masuoka, Lorianne; Lee, Ernestine A.; Hestir, Kevin F.; Chu, Keting; Bosch, Elizabeth; Hallenbeck, Robert; Williams, Lewis T.; Lin, Haishan; Behrens, Dirk (Five Prime Therapeutics, Inc., USA). PCT Int. Appl. WO 2005105840 A2 20051110, 192 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-US10760 20050328. PRIORITY: US 2004-2004/PV557092 20040326.

AB Disclosed are newly discovered CD40 variant mols., their polypeptide sequences, and the polynucleotides encoding the polypeptide sequences.

Also provided are procedures for producing such polypeptides by recombinant techniques employing, for example, vectors and host cells. Also disclosed are methods for utilizing such polypeptides and modulators thereof for the treatment of diseases, including cancer, immune diseases, infectious diseases, and ischemic diseases.

L5 ANSWER 4 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
2005:1106870 Document No. 143:365659 Bi-specific antibody moieties for targeting cells involved in allergic-type reactions. Levi-Schaffer, Francesca; Bachelet, Ido; Munitz, Ariel; Moretta, Lorenzo; Moretta, Alessandro (Yissum Research Development Company of the Hebrew University of Jerusalem, Israel). PCT Int. Appl. WO 2005095460 A2 20051013, 85 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-IL358 20050330. PRIORITY: US 2004-2004/PV557377 20040330.

AB The authors disclose bispecific antibody moieties aimed at inhibiting mast cells, eosinophils and/or basophils, and thus, at inhibiting allergy-type reactions. In particular, the bispecific moieties are directed to two targets present in the same cell. One target is the inhibitory receptor IRp60 (CD300A/LMIR1) and the second target is a cell-specific activator, e.g., IgE, cKIT, **Fc**.epsilon.RI, IL5R or CCR3. Binding of the bispecific antibody to its targets results in the induction of an inhibitory pathway.

L5 ANSWER 5 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
2005:1026832 Document No. 143:320232 Intein-based self-cleaving affinity tags for the expression and engineering of target proteins and methods of use. Wood, David W.; Hsii, Judy; Oak, Seachol; Contreras, Lydia; Chestnut, John (The Trustees of Princeton University, USA; Invitrogen Corporation). PCT Int. Appl. WO 2005086654 A2 20050922, 174 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-US5763 20050224. PRIORITY: US 2004-2004/PV548092 20040227.

AB The present invention relates to compns. and methods relating to development of modified inteins comprising one or more topoisomerase recognition sequences and the corresponding topoisomerase proteins and/or one or more recombination sites and the corresponding recombination proteins systems for use in affinity-based protein expression systems. In particular embodiments, the coding sequences for Mycobacterium tuberculosis mini cleaving (ΔI-CM) intein are modified to incorporate Topo recombination site and/or Gateway recombination site to facilitate one-step cloning for expression vector construction. The self-cleaving rate of these modified intein recombinant proteins, in particular, thymidine kinase or acid FGF **fusion** protein containing purification affinity-tags, are controllable by temperature and pH. The method is useful for protein high-throughput applications, proteomics directed evolution, drug discovery and many other areas.

L5 ANSWER 6 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
2005:371384 Document No. 142:424868 Escherichia coli hipA gene

characterizations and compositions and methods for generation of positive and negative selection vectors. Hill, Thomas; Chestnut, Jon; Leong, Louis (Invitrogen Corporation, USA). PCT Int. Appl. WO 2005038003 A2 20050428, 142 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US34119 20041015. PRIORITY: US 2003-2003/PV511509 20031016.

AB The present invention relates to the mol. characterization of the hipA gene of Escherichia coli and the hipA7 mutant thereof. The invention relates to compns., methods and kits for cloning and expression selection systems which employ the toxic gene hipA of the HipA/HipB operon of E.coli. The present invention addnl. provides compns. and methods for the development of hipA and mutants thereof as neg. and pos. selection vectors. Recombination sites suitable for use in the present invention include, attB sites, attP sites, attL sites, attR sites, lox sites, psi sites, tnpI sites, dif sites, cer sites, and frt sites. Suitable recombination proteins for use in the present invention include Int, IHF, Xis, Fis, Hin, Gin, Cin, Tn3, resolvase, TndX, XerC and XerD. The present invention also relates to the cloning of nucleic acid fragments using such neg. and pos. selection vectors by conventional recombinant DNA and recombinational cloning methods such as those employing recombination and/or topoisomerase proteins.

L5 ANSWER 7 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

2005:158690 Document No. 142:257317 Method for detecting transient ligand interactions. Lalev, Atanas Iliev; Greenblatt, Jack Frederick (Can.). PCT Int. Appl. WO 2005016956 A1 20050224, 125 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-CA1448 20040730. PRIORITY: US 2003-2003/PV49481U 20030814; US 2004-2004/PV54549C 20040219; CA 2004-2463301 20040422; US 2004-2004/PV566396 20040430.

AB The invention relates to methods and kits for separating, and optionally analyzing, substoichiometrically interacting ligands from a high abundance ligand of interest in an affinity matrix system. The methods comprise immobilizing a complex of a first and second ligand to an affinity matrix, wherein the second ligand is bound to the matrix, and subsequently eluting the first ligand from the matrix. In addition, the methods and kits can be used for drug discovery. RNA polymerase II complexes were immobilized on IgG beads via a protein A-tagged subunit of the core complex. The immobilized complex was treated with elution buffer containing 0.4 M KCl to sep. the transcription factors into the liquid phase. The transcription factors were analyzed by mass spectrometry.

L5 ANSWER 8 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

2004:817923 Document No. 141:330784 **Chimeric proteins** comprising Ig **Fc** domain and receptor ligand-binding domain or ligand receptor-binding domain for treating autoimmune disease, AIDS, transplant rejection and inflammation. Walczak, Henning (Apogenix Biotechnology A.-G., Germany). PCT Int. Appl. WO 2004085478 A2 20041007, 44 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO,

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AB The invention relates to **fusion** proteins comprising at least a first domain and a second domain selected from a constant **Fc** Ig domain. The first domain is a ligand-binding domain of receptor or a receptor-binding domain of ligand. The receptor is e.g. death receptor, growth factor receptor, cytokine receptor, CD95, TRAIL receptor, TNF receptor, or VEGF receptor; and the ligand is e.g. death ligand, growth factor, cytokine, CD95 ligand, TRAIL, TNF, VEGF or IL-15. These **fusion** proteins are useful for prophylaxis and/or treatment of autoimmune disease, AIDS, heart disease, myocardial infarction, graft vs. host disease, transplant rejection, spinal cord injury, paraplegia, sepsis, hepatitis, inflammation, ischemic reperfusion injury and renal disorders.

L5 ANSWER 9 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

2004:308529 Document No. 140:333599 Gene expression profile of human and mouse genes in atopic dermatitis and psoriasis patients and its use for diagnosis, therapy, and drug screening. Itoh, Mikito; Ogawa, Kaoru; Shinagawa, Akira; Sudo, Hajime; Ogawa, Hideoki; Ra, Chisei; Mitsuishi, Kouichi (Genox Research, Inc., Japan; Juntendo University). PCT Int. Appl. WO 2004031386 A1 20040415, 611 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2003-JP9808 20030801. PRIORITY: JP 2002-229318 20020806; JP 2003-136543 20030514.

AB This invention provides gene expression profile between a rash site and a no-rash site in a patient with atopic dermatitis or a patient with psoriasis. The invention also provides gene expression profile between a no-rash site in such a disease and a normal subject. Animal models, particularly mouse for those diseases are also claimed. The gene expression profile provided in this invention can be used for diagnosis, therapy, and drug screening for atopic dermatitis and psoriasis.

L5 ANSWER 10 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

2003:656809 Document No. 139:196279 **Chimeric proteins** comprising autoantigen epitope and effector molecule epitope for preventing and treating autoimmune diseases. Zocher, Marcel; Dreier, Torsten; Baeuerle, Patrick (Micromet A.-G., Germany). PCT Int. Appl. WO 2003068822 A2 20030821, 141 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-EP1389 20030212. PRIORITY: EP 2002-3332 20020213.

AB The present invention relates to a (poly)peptide construct consisting of at least two domains of at least two pluralities of domains wherein one of said domains or pluralities of domains comprises a de-immunized autoreactive antigen or (a) fragment(s) thereof specifically recognized by the Ig receptors of an autoreactive B-cells and wherein a/the further domain or plurality of domains comprises an effector mol. capable of interacting with and/or of activating NK-cells, T-cells, macrophages, monocytes and/or granulocytes. Preferably, said (poly)peptide construct consisting of at least two domains comprises a de-immunized autoreactive

antigen or (a) fragment which is MOG or (a) fragment(s) thereof and a second domain comprising an effector mol. is an anti-CD3 receptor or an **Fc**-part of an Ig. The invention also relates to compns. comprising the compds. of the invention. Described is also the use of the afore-mentioned (poly)peptide construct and further compds. for the preparation of a pharmaceutical composition for the treatment and/or prevention of an autoimmune disease. In addition, the present invention relates to method for treating, ameliorating and/or preventing of an autoimmune disease. Thus, MOG-CD3, MOG-**Fc**, mutated MOG-**Fc** and AchR-**Fc** **fusion** proteins were prepared for eliminating autoreactive B cells.

L5 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

2003:173831 Document No. 138:183547 Affinity tag modified particles. Bamdad, Cynthia C. (Minerva Biotechnologies Corporation, USA). PCT Int. Appl. WO 2003018846 A1 20030306, 44 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US27952 20020830. PRIORITY: US 2001-2001/PV316510 20010831.

AB The present invention provides methods, assays, kits, and components for the detection and anal. of binding between various biol. or chemical species, as well as techniques for facilitating the attachment of various biol. or chemical species to a particle. In some cases, particles having the ability to emit electromagnetic radiation within a narrow wavelength band, for example, semiconductor nanocrystals, are attached to a substrate or a structure, such as a mol., a particle, a fluid sample, a cell, or a tissue. The attachment may be a direct attachment or an indirect attachment, for example, an attachment comprising an affinity tag/recognition entity interaction. The particles may then be further used to assay biol. or chemical entities, or combined with other detection techniques.

L5 ANSWER 12 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

2003:492546 Document No. 139:65762 Polypeptide immobilization with reactant ligands to make protein chips. Mrksich, Milan; Hodneland, Christian (USA). U.S. Pat. Appl. Publ. US 2003119054 A1 20030626, 57 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-923760 20010807.

AB A substrate comprises a surface, and a plurality of moieties, on at least a portion of the surface. The moieties are moieties of formula: Surf-L-Q-T; where T comprises a reactant ligand, and Surf designates where the moiety attaches to the surface. The substrate can be made into a protein chip by the reaction of a reactant ligand and a **fusion** polypeptide, where the **fusion** polypeptide includes a capture polypeptide moiety which corresponds to the reactant ligand. Glutathione-S-transferase-hemagglutinin A **fusion** protein was immobilized on gold-coated surfaces having self-assembled monolayers of a hydroquinone-glutathione-EG5-alkanethiol (preparation given; as immobilizable reactant ligand for GST) and an alkanethiol terminated in penta(ethylene glycol) (for prevention of nonspecific adsorption of protein).

L5 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

2003:203313 Document No. 138:233055 Protein and cDNA sequences of human and mouse interleukin 21 receptor MU-1 involved in the STAT5 signaling pathway, and their therapeutic use in inhibiting immune response. Carter, Laura; Whitters, Matthew J.; Collins, Mary; Young, Deborah A.; Donaldson, Debra D.; Lowe, Leslie D.; Unger, Michelle (USA). U.S. Pat. Appl. Publ. US 2003049798 A1 20030313, 26 pp., Cont.-in-part of U.S. Ser. No. 569,384. (English). CODEN: USXXCO. APPLICATION: US 2001-972218 20011004. PRIORITY: US 1998-40005 19980317; US 2000-2000/560766 20000428; US 2000-2000/569384 20000511.

AB Polynucleotides encoding the MU-1 hematopoietin receptor superfamily chain and fragments thereof are disclosed. Specifically, the protein and cDNA sequences for human and mouse interleukin 21 receptor MU-1 are provided. The invention also relates to recombinant production of MU-1 proteins. The invention also relates to tissue distribution of human and mouse cytokine receptor MU-1. The invention demonstrated that signaling through MU-1 results in phosphorylation of STAT5. MU-1 proteins and methods for their production are also disclosed.

L5 ANSWER 14 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
2003:449849 Document No. 139:35097 Cytokine receptor zalpha11, polynucleotides and antibodies for drug screening and diagnosis/treatment of autoimmune diseases, cancer and infections. Presnell, Scott R.; Conklin, Darrell C.; Novak, Julia E.; Hammond, Angela K. (Zymogenetics, Inc., USA). U.S. US 6576744 B1 20030610, 83 pp. (English). CODEN: USXXAM. APPLICATION: US 1999-404641 19990923. PRIORITY: US 1998-PV100896 19980923; US 1999-PV123546 19990309; US 1999-PV142574 19990706.
AB Novel polypeptides, polynucleotides encoding the polypeptides, and related compns. and methods are disclosed for zalpha11, a novel cytokine receptor. The polypeptides may be used within methods for detecting ligands that stimulate the proliferation and/or development of hematopoietic, lymphoid and myeloid cells in vitro and in vivo. Ligand-binding receptor polypeptides can also be used to block ligand activity in vitro and in vivo. The polynucleotides encoding zalpha11, are located on chromosome 16, and can be used to identify a region of the genome associated with human disease states. The present invention also includes methods for producing the protein, uses therefor and antibodies thereto.

L5 ANSWER 15 OF 35 MEDLINE on STN DUPLICATE 1
2003241537. PubMed ID: 12764109. The growth arrest-specific gene product Gas6 promotes the survival of human oligodendrocytes via a phosphatidylinositol 3-kinase-dependent pathway. Shankar Sai Latha; O'Guin Kathleen; Cammer Michael; McMorris F Arthur; Stitt Trevor N; Basch Ross S; Varnum Brian; Shafit-Zagardo Bridget. (Department of Pathology, Albert Einstein College of Medicine, Bronx, New York 10461, USA.) The Journal of neuroscience : the official journal of the Society for Neuroscience, (2003 May 15) Vol. 23, No. 10, pp. 4208-18. Journal code: 8102140. E-ISSN: 1529-2401. Pub. country: United States. Language: English.
AB Microarray analysis revealed that transcripts for the Axl and Mer receptor tyrosine kinases are expressed at high levels in O4+-immunopanned oligodendrocytes isolated from second trimester human fetal spinal cord. In humans the sole known ligand for the Axl/Rse/Mer kinases is growth arrest-specific gene 6 (Gas6), which in the CNS is secreted by neurons and endothelial cells. We hypothesized that Gas6 is a survival factor for oligodendrocytes and receptor activation signals downstream to the phosphatidylinositol 3 (PI3)-kinase/Akt pathway to increase cell survival in the absence of cell proliferation. To test this hypothesis, we grew enriched human oligodendrocytes for 6 d on a monolayer of NIH3T3 cells stably expressing Gas6. CNP+ oligodendrocytes on Gas6-secreting 3T3 cells had more primary processes and arborizations than those plated solely on 3T3 cells. Also, a twofold increase in CNP+ and **MBP+** oligodendrocytes was observed when they were plated on the Gas6-secreting cells. The effect was abolished in the presence of Axl-**Fc** but remained unchanged in the presence of the irrelevant receptor **fusion** molecule TrkA-**Fc.** A significant decrease in CNP+/TUNEL+ oligodendrocytes was observed when recombinant human Gas6 (rhGas6) was administered to oligodendrocytes plated on poly-L-lysine, supporting a role for Gas6 signaling in oligodendrocyte survival during a period of active myelination in human fetal spinal cord development. PI3-kinase inhibitors blocked the anti-apoptotic effect of rhGas6, whereas a MEK/ERK inhibitor had no effect. Thus Gas6 sustains human fetal oligodendrocyte viability by receptor activation and downstream signaling via the PI3-kinase/Akt pathway.

L5 ANSWER 16 OF 35 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on

STN

2003:161748 The Genuine Article (R) Number: 640WZ. Conserved protein kinases encoded by herpesviruses and cellular protein kinase cdc2 target the same phosphorylation site in eukaryotic elongation factor 1 delta. Kawaguchi Y (Reprint); Kato K; Tanaka M; Kanamori M; Nishiyama Y; Yamanashi Y. Nagoya Univ, Sch Med, Dis Mechanism & Control Res Inst, Virol Lab, Showa Ku, 65 Tsurumai Cho, Nagoya, Aichi 4668550, Japan (Reprint); Nagoya Univ, Sch Med, Dis Mechanism & Control Res Inst, Virol Lab, Showa Ku, Nagoya, Aichi 4668550, Japan; Tokyo Med & Dent Univ, Inst Med Res, Dept Cell Regulat, Bunkyo Ku, Tokyo 1138510, Japan; Japan Sci & Technol Corp, PRESTO, Tokyo 1900012, Japan. JOURNAL OF VIROLOGY (FEB 2003) Vol. 77, No. 4, pp. 2359-2368. ISSN: 0022-538X. Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Earlier studies have shown that translation elongation factor 1delta (EF-1delta) is hyperphosphorylated in various mammalian cells infected with representative alpha-, beta-, and gammaherpesviruses and that the modification is mediated by conserved viral protein kinases encoded by herpesviruses, including UL13 of herpes simplex virus type 1 (HSV-1), UL97 of human cytomegalovirus, and BGLF4 of Epstein-Barr virus (EBV). In the present study, we attempted to identify the site in EF-1delta associated with the hyperphosphorylation by the herpesvirus protein kinases. Our results are as follows: (i) not only in infected cells but also in uninfected cells, replacement of the serine residue at position 133 (Ser-133) of EF-1delta by alanine precluded the posttranslational processing of EF-1delta, which corresponds to the hyperphosphorylation. (ii) A purified **chimeric protein** consisting of maltose binding protein (**MBP**) fused to a domain of EF-1delta containing Ser-133 (**MBP**-EFWt) is specifically phosphorylated in in vitro kinase assays by purified recombinant UL13 fused to glutathione S-transferase (GST) expressed in the baculovirus system. In contrast, the level of phosphorylation by the recombinant UL13 of **MBP**-EFWt carrying an alanine replacement of Ser-133 (**MBP**-EFS133A) was greatly impaired. (iii) **MBP**-EFWt is also specifically phosphorylated in vitro by purified recombinant BGLF4 fused to GST expressed in the baculovirus system, and the level of phosphorylation of **MBP**-EFS133A by the recombinant BGLF4 was greatly reduced. (iv) The sequence flanking Ser-133 of EF-1delta completely matches the consensus phosphorylation site for a cellular protein kinase, cdc2, and in vitro kinase assays revealed that purified cdc2 phosphorylates Ser-133 of EF-1delta. (v) As observed with EF-1delta, the casein kinase IIbeta subunit (CKIIbeta) was specifically phosphorylated by UL13 in vitro, while the level of phosphorylation of CKIIbeta by UL13 was greatly diminished when a serine residue at position 209, which has been reported to be phosphorylated by cdc2, was replaced with alanine. These results indicate that the conserved protein kinases encoded by herpesviruses and a cellular protein kinase, cdc2, have the ability to target the same amino acid residues for phosphorylation. Our results raise the possibility that the viral protein kinases mimic cdc2 in infected cells.

L5 ANSWER 17 OF 35 MEDLINE on STN DUPLICATE 2

2003334043. PubMed ID: 12847249. Modular organization of the carboxyl-terminal, globular head region of human C1q A, B, and C chains. Kishore Uday; Gupta Sanjeev K; Perdikoulis Michael V; Kojouharova Mihaela S; Urban Britta C; Reid Kenneth B M. (Medical Research Council Immunochemistry Unit, Department of Biochemistry, University of Oxford, Oxford, United Kingdom.. ukishore@hammer.imm.ox.ac.uk) . Journal of immunology (Baltimore, Md. : 1950), (2003 Jul 15) Vol. 171, No. 2, pp. 812-20. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The first step in the activation of the classical complement pathway, by immune complexes, involves the binding of the globular heads of C1q to the **Fc** regions of aggregated IgG or IgM. Located C-terminal to the collagen region, each globular head is composed of the C-terminal halves of one A (ghA), one B (ghB), and one C chain (ghC). To dissect their

structural and functional autonomy, we have expressed ghA, ghB, and ghC in Escherichia coli as soluble proteins linked to maltose-binding protein (**MBP**). The affinity-purified **fusion** proteins (**MBP**-ghA, -ghB, and -ghC) bound differentially to heat-aggregated IgG and IgM, and also to three known C1q-binding peptides, derived from HIV-1, HTLV-I, and beta-amyloid. In the ELISAs, the **MBP**-ghA bound to heat-aggregated IgG and IgM as well as to the HIV-1 gp41 peptide; the **MBP**-ghB bound preferentially to IgG rather than IgM, in addition to binding beta-amyloid peptide, whereas the **MBP**-ghC showed a preference for IgM and the HTLV-I gp21 peptide. Both **MBP** -ghA and **MBP**-ghB also inhibited C1q-dependent hemolysis of IgG- and IgM-sensitized sheep erythrocytes. However, for IgM-coated erythrocytes, **MBP**-ghC was a better inhibitor of C1q than **MBP**-ghB. The recombinant forms of ghA, ghB, and ghC also bound specifically to apoptotic PBMCs. We conclude that the C1q globular head region is likely to have a modular organization, being composed of three structurally and functionally independent modules, which retains multivalency in the form of a heterotrimer. The heterotrimeric organization thus offers functional flexibility and versatility to the whole C1q molecule.

L5 ANSWER 18 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

2004:195882 Document No.: PREV200400196441. The growth arrest specific gene product gas6 promotes the survival of human oligodendrocytes through a PI3-Kinase-dependent pathway. Shankar, S. L. [Reprint Author]; O'Guin, K. [Reprint Author]; Cammer, M.; McMorris, F.; Stitt, T. N.; Basch, R. S.; Varnum, B.; Shafit-Zagardo, B. [Reprint Author]. Dept. Pathol., AECOM, Bronx, NY, USA. Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 227.6. http://sfn.scholarone.com. e-file.
Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.
Language: English.

AB Microarray analysis revealed that transcripts for the Axl and Mer receptor tyrosine kinases are expressed at high levels in O4+ oligodendrocytes isolated from second trimester human fetal spinal cord. In humans, the sole known ligand for the Axl/Rse/Mer kinases is growth-arrest specific gene 6 (Gas6), which in the CNS is secreted by neurons and endothelial cells. We hypothesized that Gas6 is a survival factor for oligodendrocytes, and receptor activation signals downstream to the PI3 kinase/Akt pathway to increase cell survival in the absence of cell proliferation. To test this enriched human oligodendrocytes were grown for six days on a monolayer of NIH3T3 cells stably expressing Gas6. CNP+ oligodendrocytes on Gas6-secreting 3T3 cells had more primary processes and arborizations than those plated solely on 3T3 cells. Also, a two-fold increase in CNP+ and **MBP**+ oligodendrocytes was observed when plated on the Gas6-secreting cells. The effect was abolished in the presence of Axl-**Fc** but remained unchanged in the presence of the irrelevant receptor **fusion** molecule TrkA-**Fc.** A significant decrease in CNP+/TUNEL+ oligodendrocytes was observed when recombinant human Gas6 (rhGas6) was administered to oligodendrocytes plated on poly-L-lysine supporting a role for Gas6 signaling in oligodendrocyte survival during a period of active myelination in human fetal spinal cord development. PI3-kinase inhibitors blocked the anti-apoptotic effect of rhGas6, while a MEK/ERK inhibitor had no effect. Thus, Gas6 sustains human fetal oligodendrocyte viability by receptor activation and downstream signaling through the PI3-kinase/Akt pathway.

L5 ANSWER 19 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

2002:754535 Document No. 137:277811 Human cytokine receptor Zcytor16, polynucleotides, **chimeric proteins**, and antibodies for diagnosis and therapy of inflammation and cancer. Presnell, Scott R.; Xu, Wenfeng; Kindsvogel, Wayne; Chen, Zhi; Hughes, Steven D. (Zymogenetics, Inc., USA). PCT Int. Appl. WO 2002077174 A2 20021003, 268 pp. DESIGNATED

STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US8811 20020322. PRIORITY: US 2001-2001/PV279222 20010327.

AB The present invention provides a new human cytokine receptor designated as "Zcytor16", its chimeric or heterodimeric or multimeric derivs., polynucleotides, and antibodies. These Zcytor16 cytokine receptor related mols. are useful in both basic research and as therapeutics for treating and diagnosing inflammation, immune disease, infection, anemia, hematopoietic and other cancers.

L5 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

2002:595105 Document No. 137:153813 Generation and identification of monoclonal antibodies to human antigens. Nancy, Chang (Tanox, Inc., USA). PCT Int. Appl. WO 2002061389 A2 20020808, 22 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US2796 20020201. PRIORITY: US 2001-2001/PV265701 20010201.

AB A method of determining the antigens encoded by a genomic or cDNA library is disclosed. Dendritic or other antigen presenting cells are transfected with DNA fragments in a vector which includes a signal peptide coding sequence and an sequence which encodes a peptide binding to a receptor on the antigen presenting cell. The expressed DNA fragments are secreted under control of the signal peptide, and bind to a cell surface receptor. The antigen presenting cells are used to generate monoclonal antibodies. The monoclonal antibodies may be screened by cloning the same fragments into a display vector containing a transmembrane domain thereby displaying the expressed proteins on the surface of a host cell. The monoclonal are screened against these displayed proteins for a pos. match.

L5 ANSWER 21 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

2002:293666 Document No. 136:320304 Production of concatenated nucleic acid sequences in head-to-tail orientation. Winter, Gregory; Jespers, Laurent; Lasters, Ignace; Wang, Peter (Medical Research Council, UK). PCT Int. Appl. WO 2002030945 A2 20020418, 73 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-GB4615 20011015. PRIORITY: GB 2000-25144 20001013.

AB An in vitro method for constructing a concatenated head-to-tail repertoire of target nucleic acid sequences is revealed. In particular, the method relates to cycles of concatenation whereby after a single cycle of concatenation, not more than two identical copies of each target nucleic acid sequences are linked together head-to-tail on the same mol. of DNA. The present method ensures that each mol. of a concatenated repertoire is derived from a single template target sequence of the starting repertoire. Advantageously, the method involves introducing two single-strand nicks, one at each of the 5' ends of the target nucleic acid sequence, such that the top and bottom strands of the target nucleic acid sequence are

converted into 5'-overhangs; incubating the resulting nicked DNA sequence with a nucleic acid polymerase under conditions which result in filling of the 5'-overhangs to generate blunt ends (thereby creating two identical copies of the target nucleic acid sequence on the same mol. of DNA); and incubating the resulting blunt-ended DNA sequence with a nucleic acid ligase to covalently link the two copies of the target nucleic acid sequence in ahead-to-tail orientation. The invention also related to biopanning of peptide libraries on erythropoietin receptor-**Fc** or ferritin.

L5 ANSWER 22 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
2002:755100 Document No. 137:274170 A new member of the disintegrin family, zdint5, useful for modulating extracellular matrix interaction as anti-angiogenic factors. Holloway, James L.; Sheppard, Paul O.; Yamamoto, Gayle (USA). U.S. Pat. Appl. Publ. US 2002142439 A1 20021003, 37 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-781080 20010209. PRIORITY: US 2000-2000/PV181511 20000210.

AB The present invention relates to polynucleotide and polypeptide mols., and variants thereof, for zdint5, a novel member of the Disintegrin Proteases. In particular, a member of the METH subfamily of proteins designated zdint5 METHs (Metalloprotease and Thrombospondin-1 repeat proteins) subfamily, designated as zdint5, is identified by domain sequence homol. search. Domains of zdint5 include: a metalloprotease domain, and two TSP1-like (Thrombospondin-1) domains. The polypeptides, and polynucleotides encoding them, are cell-cell interaction modulating and may be used for delivery and therapeutics. The present invention also includes antibodies to the zdint5 polypeptides.

L5 ANSWER 23 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
2003:468095 Document No. 139:357756 **Chimeric proteins**: A novel approach for eliminating specific cell populations for targeted human therapy. Ben-Yehudah, Ahmi; Belostotsky, Ruth; Aqeilan, Rami; Azar, Yehudith; Steinberger, Ida; Fishman, Ala; Nechushtan, Amotz; Yarkoni, Shai; Lorberboum-Galski, Haya (Department of Cellular Biochemistry and Human Genetics, Hebrew University-Hadassah Medical School, Jerusalem, 91120, Israel). Cellular and Molecular Mechanisms of Toxin Action, Volume 4, 148-167. Editor(s): Lazarovici, Philip. Taylor & Francis Ltd.: London, UK. (English) 2002. CODEN: 64JPAO.

AB A review. One of the most widely used toxins in **chimeric proteins** is the bacterial toxin Pseudomonas exotoxin (PE) produced by the bacterium Pseudomonas aeruginosa. Various **chimeric proteins** were constructed using two modified forms of the PE toxin: (a) in which Domain I is deleted, generating the PE40 truncated form of PE, (b) by introducing mutations into the binding domain (Domain I) of PE (at amino acid positions 57, 246, 247, 249, all substituted by Glu) to generate the PE664GOu mutated form of PE. The authors designed a number of **chimeric proteins** for the cure of unrelated disorders: autoimmune diseases, allergy and cancer. For each of these diseases the authors constructed **chimeric proteins** carrying a specific targeting moiety: Interleukin-2 (IL2) for eliminating activated T cells involved in many human diseases, myelin basic protein (**MBP**) for therapy of multiple sclerosis (MS), **Fc**.epsilon. for use in the treatment of asthma and other allergic disorders and gonadotropin releasing hormone (GnRH) for targeting adenocarcinomas.

L5 ANSWER 24 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
2001:435310 Document No. 135:41773 Use of multiple recombination sites with unique specificity in recombinational cloning. Cheo, David; Brasch, Michael A.; Temple, Gary F.; Hartley, James L.; Byrd, Devon R. N. (USA). PCT Int. Appl. WO 2001042509 A1 20010614, 357 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,

TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US33546 20001211. PRIORITY: US 1999-PV169983 19991210; US 2000-PV188020 20000309.

AB The present invention provides compns. and methods for recombinational cloning. The compns. include vectors having multiple recombination sites with unique specificity. The methods permit the simultaneous cloning of two or more different nucleic acid mols. In some embodiments the mols. are fused together while in other embodiments the mols. are inserted into distinct sites in a vector. The invention also generally provides for linking or joining through recombination a number of mols. and/or compds. (e.g., chemical compds., drugs, proteins or peptides, lipids, nucleic acids, carbohydrates, etc.) which may be the same or different. Such mols. and/or compds. or combinations of such mols. and/or compds. can also be bound through recombination to various structures or supports according to the invention.

L5 ANSWER 25 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

2001:792260 Document No. 135:341166 Use of modified tethers in screening compound libraries. Dower, William J.; Gates, Christian M.; Heinkel, Gregory L.; Lalonde, Guy; Mattheakis, Larry C.; Paddon, Christopher J.; Schatz, Peter J. (Glaxo Wellcome Inc., USA). U.S. US 6309842 B1 20011030, 50 pp., Cont.-in-part of U.S. 5,958,703. (English). CODEN: USXXAM. APPLICATION: US 1997-977378 19971124. PRIORITY: US 1996-758307 19961203.

AB The invention provides methods for screening libraries of complexes for compds. having a desired property, especially, the capacity to agonize, bind to, or antagonize a cellular receptor. The complexes in such libraries comprise a compound under test, a tag recording at least one step in synthesis of the compound, and a tether susceptible to modification by a reporter mol. Modification of the tether is used to signify that a complex contains a compound having a desired property. The tag can be decoded to reveal at least one step in the synthesis of such a compound A method of screening compds. for capacity to transduce a signal through a cellular receptor is claimed, comprising providing a plurality of supports, each support bearing multiple copies of a compound under test, and a tether susceptible to modification by a reporter mol.; contacting the supports with cells having a receptor and a DNA fragment encoding the reporter mol.; freeing a portion of the multiple copies of each of the compds. under test from the supports, whereby at least one compound transduces a signal through the receptor of a cell causing expression of the reporter mol., which reporter mol. is released from the cell and modifies the tether of the support from which a portion of the multiple copies of the compound transducing the signal was freed; and isolating the support having the modified tether, which support bears the compound transducing the signal.

L5 ANSWER 26 OF 35 MEDLINE on STN

2002016006. PubMed ID: 11430750. A solubility-enhancement tag (SET) for NMR studies of poorly behaving proteins. Zhou P; Lugovskoy A A; Wagner G. (Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA 02115, USA.) Journal of biomolecular NMR, (2001 May) Vol. 20, No. 1, pp. 11-4. Journal code: 9110829. ISSN: 0925-2738. Pub. country: Netherlands. Language: English.

AB Protein-**fusion** constructs have been used with great success for enhancing expression of soluble recombinant protein and as tags for affinity purification. Unfortunately the most popular tags, such as GST and **MBP**, are large, which hinders direct NMR studies of the **fusion** proteins. Cleavage of the **fusion** proteins often re-introduces problems with solubility and stability. Here we describe the use of N-terminally fused protein G (B1 domain) as a non-cleavable solubility-enhancement tag (SET) for structure determination of a dimeric protein complex. The SET enhances the solubility and stability of the **fusion** product dramatically while not interacting directly with the protein of interest. This approach can be used for structural

characterization of poorly behaving protein systems, and would be especially useful for structural genomics studies.

L5 ANSWER 27 OF 35 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

2000:323738 Document No.: PREV200000323738. Kinetics of T-cell receptor binding by bivalent HLA-DRcntdotpeptide complexes that activate antigen-specific human T-cells. Appel, Heiner; Gauthier, Laurent; Pyrdol, Jason; Wucherpfennig, Kai W. [Reprint author]. Dept. of Cancer Immunology and AIDS, Dana-Farber Cancer Institute, Boston, MA, 02115, USA. Journal of Biological Chemistry, (January 7, 2000) Vol. 275, No. 1, pp. 312-321. print.
CODEN: JBCHA3. ISSN: 0021-9258. Language: English.

AB Monovalent major histocompatibility complex-peptide complexes dissociate within seconds from the T-cell receptor (TCR), indicating that dimerization/multimerization may be important during early stages of T-cell activation. Soluble bivalent HLA-DR2cntdotmyelin basic protein (**MBP**) peptide complexes were expressed by replacing the F(ab) arms of an IgG2a antibody with HLA-DR2cntdotMBP peptide complexes. The binding of bivalent HLA-DR2cntdotpeptide complexes to recombinant TCR was examined by surface plasmon resonance. The bivalent nature greatly enhanced TCR binding and slowed dissociation from the TCR, with a t1/2 of 2.1 to 4.6 min. Soluble bivalent HLA-DR2cntdotMBP peptide complexes activated antigen-specific T-cells in the absence of antigen presenting cells. In contrast, soluble antibodies to the TCRcntdotCD3 complex were ineffective, indicating that they failed to induce an active TCR dimer. TCR/CD3 antibodies induced T-cell proliferation when bound by antigen presenting cells that expressed **Fc** receptors. In the presence of dendritic cells, bivalent HLA-DR2cntdotMBP peptide complexes induced T-cell activation at >100-fold lower concentrations than TCR/CD3 antibodies and were also superior to peptide or antigen. These results demonstrate that bivalent HLA-DRcntdotpeptide complexes represent effective ligands for activation of the TCR. The data support a role for TCR dimerization in early TCR signaling and kinetic proofreading.

L5 ANSWER 28 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

1999:549393 Document No. 131:183867 Monovalent, multivalent, and multimeric MHC binding domain **fusion** proteins and conjugates, and uses therefor. Wucherpfennig, Kai W.; Strominger, Jack L. (President and Fellows of Harvard College, USA). PCT Int. Appl. WO 9942597 A1 19990826, 113 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US3603 19990219. PRIORITY: US 1998-PV75351 19980219.

AB The present invention is directed to the design, production, and use of monovalent, multivalent and multimeric major histocompatibility complex binding domain **fusion** proteins and conjugates. The MHC **fusion** proteins and conjugates may comprise MHC class II α or β chain (HLA-DRA*0101, HLA-DRA*0102, HLA-DQA1*0301, HLA-DRB1*01, etc.), leucine zipper domain of Fos or Jun, linker peptide, yeast σ-mating factor secretion signal, human myelin basic protein tag, IgG or IgE or IgM **Fc**, and optionally cytotoxic substance (human desmoglein 3 protein peptide). The MHC binding domain **fusion** proteins and conjugates are useful for diagnosis and treatment of diseases associated with T cell-mediated immune response and antigen presentation, e.g. autoimmune disease, multiple sclerosis and rheumatoid arthritis. Thus, **fusion** proteins containing HLA-DR2 α chain (β chain), Fos (Jun) leucine zipper dimerization domain, VDGGGGG linker, and α-mating secretion signal were prepared, fused with IgG2a or IgM, tagged with **MBP** peptide, conjugated with bead carrier, and used

for selectively depletion of T cells.

L5 ANSWER 29 OF 35 MEDLINE on STN DUPLICATE 3
2000107505. PubMed ID: 10642893. A gene therapy or purified CTLA4IgG treatment of experimental allergic encephalomyelitis. Kawaguchi Y. (Section of Immunopathogenesis, Hokkaido University, Sapporo, Japan.) [Hokkaido igaku zasshi] The Hokkaido journal of medical science, (1999 Nov) Vol. 74, No. 6, pp. 467-75. Journal code: 17410290R. ISSN: 0367-6102. Pub. country: Japan. Language: English.
AB We examined whether multiple intraperitoneal injection of a soluble form of a **chimeric protein** consisting of an extracellular portion of cytotoxic T lymphocyte-associated protein 4 and an **Fc** portion of human IgG1(CTLA4IgG) at the initiation phase could successfully control the subsequent development of experimental allergic encephalomyelitis (EAE). We demonstrated that CTLA4IgG treatment could delay the onset and reduce the severity of EAE in early phase of disease development. More importantly, CTLA4IgG treatment significantly reduced the incidence of EAE. This was in good agreement to that spleen cells obtained from CTLA4IgG-treated animals responded poorly to myelin basic protein (**MBP**) in vitro as compared to those from human IgG-treated animals. However, the CTLA4IgG-treated mice eventually developed EAE and after all, incidence of EAE was not significantly different from that in control group. We then tested whether a gene therapy using adenovirus vector containing CTLA4IgG (Adex1CACTLA4IgG) could inhibit the development of EAE. We demonstrated that incidence and severity of EAE were significantly inhibited by a single injection of intravenous Adex1CACTLA4IgG up to 8 months. Thus, this study demonstrated the efficacy of a single dose of adenovirus-mediated gene therapy in controlling EAE as compared to repeated injection of purified CTLA4IgG proteins.

L5 ANSWER 30 OF 35 MEDLINE on STN
1998230504. PubMed ID: 9570577. Expansion of autoreactive T cells in multiple sclerosis is independent of exogenous B7 costimulation. Scholz C; Patton K T; Anderson D E; Freeman G J; Hafler D A. (Laboratory of Molecular Immunology, Department of Neurology, Brigham and Women's Hospital, Boston, MA 02115, USA.) Journal of immunology (Baltimore, Md. : 1950), (1998 Feb 1) Vol. 160, No. 3, pp. 1532-8. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
AB Multiple sclerosis (MS) is an inflammatory disease of the myelinated central nervous system that is postulated to be induced by myelin-reactive CD4 T cells. T cell activation requires an antigen-specific signal through the TCR and a costimulatory signal, which can be mediated by B7-1 or B7-2 engagement of CD28. To directly examine the activation state of myelin-reactive T cells in MS, the costimulation requirements necessary to activate myelin basic protein (**MBP**) or tetanus toxoid (TT)-reactive CD4 T cells were compared between normal controls and MS patients. Peripheral blood T cells were stimulated with Chinese hamster ovary (CHO) cells transfected either with DRB1*1501/DRA0101 chains (t-DR2) alone, or in combination with, B7-1 or B7-2. In the absence of costimulation, T cells from normal subjects stimulated with the recall antigen TT p830-843 were induced to expand and proliferate, but stimulation with **MBP** p85-99 did not have this effect. In marked contrast, T cells from patients with MS stimulated with **MBP** p85-99 in the absence of B7-1 or B7-2 signals expanded and proliferated. Thus, **MBP**-reactive CD4 T cells in patients with MS are costimulation independent and have been previously activated in vivo. These experiments provide further direct evidence for a role of activated **MBP**-specific CD4 T cells in the pathogenesis of MS.

L5 ANSWER 31 OF 35 MEDLINE on STN DUPLICATE 4
1998306049. PubMed ID: 9639558. Functional characterization of a recombinant form of the C-terminal, globular head region of the B-chain of human serum complement protein, C1q. Kishore U; Leigh L E; Eggleton P; Strong P; Perdikoulis M V; Willis A C; Reid K B. (Medical Research Council

Immunochemistry Unit, Department of Biochemistry, University of Oxford, South Parks Road, Oxford OX1 3QU, U.K.) The Biochemical journal, (1998 Jul 1) Vol. 333 (Pt 1), pp. 27-32. Journal code: 2984726R. ISSN: 0264-6021. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The first step in the activation of the classical pathway of the complement system by immune complexes involves the binding of the six globular heads of C1q to the **Fc** regions of IgG or IgM. The globular heads of C1q are located C-terminal to the six triple-helical stalks present in the molecule; each head is considered to be composed of the C-terminal halves (3x136 residues) of one A-, one B- and one C-chain. It is not known if the C-terminal globular regions, present in each of the three types of chain, are independently folded modules (with each chain having distinct binding properties towards immunoglobulins) or whether the different binding functions of C1q are dependent upon a globular structure which relies on contributions from all three chains. As a first step towards addressing this question, we have expressed the globular head region (residues 87-226) of the C1q B-chain (ghB) as a soluble **fusion** protein with maltose-binding protein (**MBP**) in Escherichia coli. The affinity purified **fusion** protein, designated **MBP**-ghB, behaved as a dimer on gel filtration and bound preferentially to aggregated IgG rather than to IgM. It could also inhibit C1q-dependent haemolysis of both IgG- and IgM-sensitized erythrocytes. After its release from **MBP**, by use of Factor Xa, the free ghB exhibited a tendency to aggregate and come out of solution. Since **MBP** is known to be a monomeric molecule, the dimerization of the **MBP**-ghB **fusion** polypeptide is probably brought about by the ghB region, perhaps through hydrophobic interactions within the ghB region. The functional behaviour of **MBP**-ghB indicates that the globular regions of C1q may adopt a modular organization, i.e. each globular head of C1q may be composed of three structurally and functionally independent domains, thus retaining multivalency in the form of a heterotrimer.

L5 ANSWER 32 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

1997:776258 Document No. 128:60727 Hematopoietic cytokine receptor Zcytor1 and its variants. Baumgartner, James W.; Foster, Donald C.; Grant, Francis J.; Sprecher, Cindy A. (Zymogenetics, Inc., USA). PCT Int. Appl. WO 9744455 A1 19971127, 85 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US8502 19970519. PRIORITY: US 1996-653740 19960523.

AB Novel DNA sequences are provided that encode proteins having the structure of a cytokine receptor including the conserved WSXWS motif. An isolated human cDNA encoding this receptor, designated Zcytor1, includes an open reading frame encoding 578 amino acids. The deduced amino acid sequence indicated that the encoded receptor belongs to the receptor subfamily that includes the G-CSF, IL-6, CNTF, IL-11, OSM, LIF, CT-1, and gp130 receptors. In addition to the WSXWS motif at residues 217-221, the receptor comprises a cytokine binding region of .apprx.200 residues, 3 fibronectin type III domains (residues 236-514), a transmembrane domain (residues 515-540), and an intracellular or signaling domain (residues 541-578). An alternatively spliced, human cDNA was also isolated, which encoded a protein with a 58-amino-acid insertion near the C-terminus of Zcytor1, and a representative mouse Zcytor1 clone was also isolated. The polypeptides are expressed at high levels in lymphoid tissue, including B-cells and T-cells. The polypeptides may be used within methods for detecting ligands that stimulate the proliferation and/or development of lymphoid and myeloid cells in vitro and in vivo. Ligand-binding receptor polypeptides can also be used to block ligand activity in vitro and in vivo.

L5 ANSWER 33 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
1997:536920 Document No. 127:160682 Protein expression system. Sgarlato, Gregory D. (Technologene Inc., USA). PCT Int. Appl. WO 9728272 A1 19970807, 193 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US1470 19970131. PRIORITY: US 1996-595043 19960131.

AB The present invention relates to improved recombinant vectors which allow for the production of **fusion** proteins. The present invention also relates to methods for the expression and purification of authentic recombinant proteins from such **fusion** proteins. In particular, the present invention relates to **fusion** proteins wherein addnl. domains and/or elements are added to the **fusion** proteins. Included in these domains and/or elements are **Fc** fragments (1) fused to proteins of interest (2) by a polypeptide comprising a hinge region (3), hydrophilic spacer (4), and a dibasic amino acid endoprotease cleavage site (5), wherein the spacer may be cleaved and then digested by carboxypeptidase B (6) to yield the authentic protein (2).

L5 ANSWER 34 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
1997:301863 Document No. 127:29792 Design, synthesis, expression, and characterization of the genes for mouse **Fc**.gamma.RIIb1 and **Fc**.gamma.RIIb2 cytoplasmic regions. Chen, Lixin; Thompson, Nancy L.; Pielak, Gary J. (Department of Chemistry, University of North Carolina, Chapel Hill, NC, 27599-3290, USA). Protein Science, 6(5), 1038-1046 (English) 1997. CODEN: PRCIEI. ISSN: 0961-8368. Publisher: Cambridge University Press.

AB The cytoplasmic regions of the mouse low-affinity **Fc**.gamma.RII isoforms, mFcγRIIb1, and mFcγRIIb2, play a key role in signal transduction by mediating different cellular functions. MFcγRIIb1 has a 94-residue cytoplasmic region, whereas mFcγRIIb2 has a 47-residue cytoplasmic region. Genes encoding the cytoplasmic regions of mFcγRIIb1 (b1-94) and mFcγRIIb2 (b2-47) were designed, synthesized, and expressed as **fusion** proteins in Escherichia coli. A sequence-specific protease, thrombin, was used to release the b1-94 peptide, which was purified by using HPLC. The b2-47 peptide was synthesized chemical CD spectropolarimetry was employed to examine the secondary structures of b1-94 and b2-47. These studies were conducted in aqueous solution, in mixts. of water and trifluoroethanol or methanol, and as a function of temperature The results indicate that the b1-94 and b2-47 structures are sensitive functions of the solvent environment, and that nonaq. solvents induce significant α-helical structure.

L5 ANSWER 35 OF 35 MEDLINE on STN DUPLICATE 5
94247422. PubMed ID: 8190127. Src family tyrosine kinase Lyn binds several proteins including paxillin in rat basophilic leukemia cells. Minoguchi K; Kihara H; Nishikata H; Hamawy M M; Siraganian R P. (Laboratory of Immunology, National Institute of Dental Research, National Institutes of Health, Bethesda, MD 20892.) Molecular immunology, (1994 May) Vol. 31, No. 7, pp. 519-29. Journal code: 7905289. ISSN: 0161-5890. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Aggregation of the high affinity IgE receptors on rat basophilic leukemia (RBL-2H3) cells results in protein tyrosine phosphorylation although the receptor has no intrinsic enzymatic activity. The Src related protein tyrosine kinase p53/56lyn present in RBL-2H3 cells could play a role in this reaction. Here we have isolated the cDNA for rat Lyn and found it to be very homologous at the amino acid level to both the human and mouse proteins. A bacterially expressed maltose binding protein-Lyn (**MBP**-Lyn) **fusion** protein was already tyrosine phosphorylated and had tyrosine kinase activity. In a filter-binding assay, **MBP**-Lyn **fusion** protein (at 0.1 microM) specifically bound to several proteins of RBL-2H3 cells. In lysates of IgE receptor-activated cells, there was increased binding of **MBP** -Lyn to 65, 72, 78 and 110 kDa tyrosine phosphorylated proteins. The 72, 78 and 110 kDa tyrosine phosphorylated proteins were precipitated by a

fusion protein containing the Lyn Src Homology 2 (SH2) domain. The 72 kDa Lyn binding protein was different from p72syk. Furthermore, paxillin, a cytoskeletal protein, was identified as one of the Lyn binding proteins. Thus **Fc** epsilon RI mediated signal transduction in RBL-2H3 cells may result from the interaction of p53/56lyn with paxillin, pp72, pp110 and other proteins.

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     (FILE 'HOME' ENTERED AT 14:31:30 ON 06 MAR 2006)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 14:31:43 ON
     06 MAR 2006
L1        718452 S FUSION OR CHIMERIC PROTEIN
L2          9070 S L1 AND FC
L3             0 S L2 AND MYELINE BASIC PROTEIN
L4            52 S L2 AND MBP
L5            35 DUP REMOVE L4 (17 DUPLICATES REMOVED)

=> s l5 and human MBP
L6             0 L5 AND HUMAN MBP

=> s l5 and IgE receptor
L7             1 L5 AND IGE RECEPTOR

=> d l7 cbib abs

L7   ANSWER 1 OF 1     MEDLINE on STN
94247422.    PubMed ID: 8190127.   Src family tyrosine kinase Lyn binds several
     proteins including paxillin in rat basophilic leukemia cells. Minoguchi K;
     Kihara H; Nishikata H; Hamawy M M; Siraganian R P. (Laboratory of
     Immunology, National Institute of Dental Research, National Institutes of
     Health, Bethesda, MD 20892. ) Molecular immunology, (1994 May) Vol. 31,
     No. 7, pp. 519-29.  Journal code: 7905289. ISSN: 0161-5890. Pub. country:
     ENGLAND: United Kingdom. Language: English.
AB   Aggregation of the high affinity IgE receptors on rat
     basophilic leukemia (RBL-2H3) cells results in protein tyrosine
     phosphorylation although the receptor has no intrinsic enzymatic activity.
     The Src related protein tyrosine kinase p53/56lyn present in RBL-2H3 cells
     could play a role in this reaction. Here we have isolated the cDNA for
     rat Lyn and found it to be very homologous at the amino acid level to both
     the human and mouse proteins. A bacterially expressed maltose binding
     protein-Lyn (MBP-Lyn) fusion protein was already
     tyrosine phosphorylated and had tyrosine kinase activity. In a
     filter-binding assay, MBP-Lyn fusion protein (at 0.1
     microM) specifically bound to several proteins of RBL-2H3 cells. In
     lysates of IgE receptor-activated cells, there was
     increased binding of MBP-Lyn to 65, 72, 78 and 110 kDa tyrosine
     phosphorylated proteins. The 72, 78 and 110 kDa tyrosine phosphorylated
     proteins were precipitated by a fusion protein containing the
     Lyn Src Homology 2 (SH2) domain. The 72 kDa Lyn binding protein was
     different from p72syk. Furthermore, paxillin, a cytoskeletal protein, was
     identified as one of the Lyn binding proteins. Thus Fc epsilon
     RI mediated signal transduction in RBL-2H3 cells may result from the
     interaction of p53/56lyn with paxillin, pp72, pp110 and other proteins.


=> s myelin basic protein
L8         36999 MYELIN BASIC PROTEIN

=> s l8 and fusion
L9           771 L8 AND FUSION

=> s l9 and Fc
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L10 35 L9 AND FC

=> dup remove l10
PROCESSING COMPLETED FOR L10
L11 23 DUP REMOVE L10 (12 DUPLICATES REMOVED)

=> d l11 1-23 cbib abs

L11 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
2006:13021 Document No. 144:101055 Protein Sp35/LINGO-1 antagonists for treatment of conditions involving demyelination. Mi, Sha; Pepinsky, R. Blake; McCoy, John (Biogen Idec Ma Inc., USA). PCT Int. Appl. WO 2006002437 A2 20060105, 183 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-US22881 20050624. PRIORITY: US 2004-2004/PV58296U 20040624; US 2004-2004/PV61729U 20041007; US 2004-2004/PV62843U 20041115; US 2005-2005/PV680475 20050513.

AB The invention provides methods of treating diseases, disorders or injuries involving demyelination and dysmyelination, including multiple sclerosis, by the administration of an Sp35/LINGO-1 antagonist. The Sp35/LINGO-1 antagonists include soluble Sp35 peptides, Sp35 **fusion** products with antibodies or antibody fragments, and Sp35 antisense polynucleotides, ribozymes, siRNA, or small hairpin RNA. The invention further claims polypeptide sequences for human Sp35 polypeptide and peptides, and a DNA sequence for an Sp35 shRNA. The human Sp35 protein contains signal sequence, a domain with 14 leucine-rich repeats, an Ig domain, a transmembrane region, and a cytoplasmic domain. The human Sp35 gene contains alternative translation start codons, so that 6 addnl. amino acids may or may not be present at the N-terminus of the Sp35 signal sequence. Rat oligodendrocyte precursor cells were infected with a lentiviral vector containing Sp35/LINGO-1 RNAi. Endogenous Sp35 expression was reduced as determined by RT-PCR and this resulted in more highly differentiated, mature oligodendrocytes compared with the control. An Sp35-**Fc fusion** protein was constructed using the extracellular region of human Sp35 and human IgG1 **Fc** region. Purified recombinant Sp35-**Fc** protein promoted differentiation of rat precursor cells into O4-expressing mature oligodendrocytes and increased the in vitro survival rate for MBP-expressing mature oligodendrocytes. Sp35-**Fc fusion** protein and Ig domain peptides of Sp35 promoted myelination in vitro in co-cultures of rat dorsal root ganglion neurons and oligodendrocytes. In vivo transplantation of Sp35-transformed cells to injured rat spinal cords resulted in more oligodendrocyte and axon myelination and less axon retraction than in the control.

L11 ANSWER 2 OF 23 MEDLINE on STN DUPLICATE 1
2005226584. PubMed ID: 15788534. Leptin increase in multiple sclerosis associates with reduced number of CD4(+)CD25+ regulatory T cells. Matarese Giuseppe; Carrieri Pietro Biagio; La Cava Antonio; Perna Francesco; Sanna Veronica; De Rosa Veronica; Aufiero Daniela; Fontana Silvia; Zappacosta Serafino. (Istituto di Endocrinologia e Oncologia Sperimentale, Consiglio Nazionale delle Ricerche (IEOS-CNR), 80131 Naples, Italy.. gmatarese@napoli.com) . Proceedings of the National Academy of Sciences of the United States of America, (2005 Apr 5) Vol. 102, No. 14, pp. 5150-5. Electronic Publication: 2005-03-23. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB We analyzed the serum and cerebrospinal fluid (CSF) leptin secretion and the interaction between serum leptin and CD4(+)CD25+ regulatory T cells (T(Regs)) in naive-to-therapy relapsing-remitting multiple sclerosis

(RRMS) patients. Leptin production was significantly increased in both serum and CSF of RRMS patients and correlated with IFN-gamma secretion in the CSF. T cell lines against human **myelin basic protein** (hMBP) produced immunoreactive leptin and up-regulated the expression of the leptin receptor (ObR) after activation with hMBP. Treatment with either anti-leptin or anti-leptin-receptor neutralizing antibodies inhibited in vitro proliferation in response to hMBP. Interestingly, in the RRMS patients, an inverse correlation between serum leptin and percentage of circulating T(Regs) was also observed. To better analyze the finding, we enumerated T(Regs) in leptin-deficient (ob/ob) and leptin-receptor-deficient (db/db) mice and observed the significant increase in T(Regs). Moreover, treatment of WT mice with soluble ObR **fusion** protein (ObR:**Fc**) increased the percentage of T(Regs) and ameliorated the clinical course and progression of disease in proteolipid protein peptide (PLP(139-151))-induced relapsing-experimental autoimmune encephalomyelitis (R-EAE), an animal model of RRMS. These findings show an inverse relationship between leptin secretion and the frequency of T(Regs) in RRMS and may have implications for the pathogenesis of and therapy for multiple sclerosis.

L11 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
2004:308529 Document No. 140:333599 Gene expression profile of human and mouse genes in atopic dermatitis and psoriasis patients and its use for diagnosis, therapy, and drug screening. Itoh, Mikito; Ogawa, Kaoru; Shinagawa, Akira; Sudo, Hajime; Ogawa, Hideoki; Ra, Chisei; Mitsuishi, Kouichi (Genox Research, Inc., Japan; Juntendo University). PCT Int. Appl. WO 2004031386 A1 20040415, 611 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2003-JP9808 20030801. PRIORITY: JP 2002-229318 20020806; JP 2003-136543 20030514.
AB This invention provides gene expression profile between a rash site and a no-rash site in a patient with atopic dermatitis or a patient with psoriasis. The invention also provides gene expression profile between a no-rash site in such a disease and a normal subject. Animal models, particularly mouse for those diseases are also claimed. The gene expression profile provided in this invention can be used for diagnosis, therapy, and drug screening for atopic dermatitis and psoriasis.

L11 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
2004:550059 Document No. 141:85148 Method for testing of activation states of protein molecules. Takahashi, Isao (Olympus Optical Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 2004191182 A2 20040708, 15 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 2002-359501 20021211.
AB The process involves (1) reaction of protein mols., whose activation states are tested, with labeled substrate mols., in which changes are induced by the action of the protein mols., (2) reaction of the substrate mols. with mols. which specifically recognize the substrate mols. before changing and/or those after changing, and (3) detection of the substrate mols. before or after changing. Preferably, the labeling substances are fluorescent substances, and the changes in the substrate mols. are measured by fluorescence correlation spectroscopy (**FCS**). The activation states (i.e., phosphorylation states) of JNK kinase was tested by reaction of JNK kinase from mouse macrophage-like cells with fluorescein isothiocyanate (FITC)-labeled glutathione S-transferase-c-Jun(1-79) **fusion** protein, and reaction of the substrates with anti-phosphoserine antibody or anti-phospho-Jun antibody.

L11 ANSWER 5 OF 23 MEDLINE on STN DUPLICATE 2
2004209928. PubMed ID: 14988414. NTB-A, a new activating receptor in T

cells that regulates autoimmune disease. Valdez Patricia A; Wang Hua; Seshasayee Dhaya; van Lookeren Campagne Menno; Gurney Austin; Lee Wyne P; Grewal Iqbal S. (Department of Immunology and Molecular Biology, Genentech Inc., South San Francisco, California 94080, USA.) The Journal of biological chemistry, (2004 Apr 30) Vol. 279, No. 18, pp. 18662-9. Electronic Publication: 2004-02-26. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB The CD28 co-stimulatory pathway is well established for T cell activation; however, results from CD28 -/- mice suggest the existence of additional co-stimulatory pathways. Here we report the further characterization of a new member of the CD2 superfamily, NTB-A, important in T cell co-stimulation. NTB-A is expressed on T cells, and its expression is up-regulated on activated cells. Triggering of NTB-A with monoclonal antibodies in the absence of CD28 signals leads to T cell proliferation and interferon-gamma secretion but not interleukin-4. Cross-linking of NTB-A also induces phosphorylation of NTB-A and the association of SAP (SLAM-associated protein), the protein absent in X-linked lymphoproliferative disease. T helper cells differentiated by cross-linking NTB-A and CD3 developed predominantly into Th1 cells not Th2 cells. In vivo blocking of NTB-A interactions with its ligands by using soluble NTB-A-**Fc fusion** protein inhibits B cell isotype switching to IgG2a and IgG3, commonly induced by Th1-type cytokines. Most important, treatment of mice with NTB-A-**Fc** delays the onset of antigen-induced experimental allergic encephalomyelitis in **myelin basic protein**-T cell receptor transgenic mice, suggesting a role in T cell-mediated autoimmune disease. Regulation of interferon-gamma secretion, and not interleukin-4 in vitro, as well as inhibition of Th1 cell-induced isotype switching and attenuation of experimental allergic encephalomyelitis indicate that NTB-A is important for Th1 responses. The observation that cross-linking of NTB-A induces T cell activation, expansion, and Th1-type cytokine production suggests NTB-A is a novel co-stimulatory receptor. The identification of NTB-A as a regulator of T cell response paves the way to provide novel therapeutic approaches for modulation of the immune response.

L11 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

2003:260853 Document No. 138:285999 Chimeric proteins comprising ITIM motif, antigen and **Fc**.epsilon.R binding peptide for treating immune diseases. Saxon, Andrew (USA). U.S. Pat. Appl. Publ. US 2003064063 A1 20030403, 51 pp., Cont.-in-part of U.S. Ser. No. 847,208. (English). CODEN: USXXCO. APPLICATION: US 2001-439 20011024. PRIORITY: US 2001-2001/847208 20010501.

AB The invention concerns bifunctional **fusion** mols., and novel, safer and more efficacious methods for the treatment of immune disorders resulting from excessive or unwanted immune responses. The invention provides methods for the suppression of type I hypersensitive (i.e., IgE-mediated) allergic conditions, methods for the prevention of anaphylactic responses that occur as a result of traditional peptide immunotherapies for allergic and autoimmune disorders, and provides novel methods for the treatment of autoimmune conditions, where the methods have reduced risk of triggering an anaphylactic response. The invention provides novel therapeutic approaches for the treatment of allergic responses, including the prevention of anaphylactic response that can occur from environmental allergen exposure. The invention also provides methods for the treatment of autoimmune disorders such as multiple sclerosis, autoimmune type I diabetes mellitus, and rheumatoid arthritis. The invention also provides methods for preventing anaphylactic response during traditional antigen therapies.

L11 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

2003:487103 Document No. 139:51605 **Fusion** proteins containing **Fc**-regions. Cherkasky, Alexander (Germany). Ger. Offen. DE 10160248 A1 20030626, 6 pp. (German). CODEN: GWXXBX. APPLICATION: DE 2001-10160248 20011207.

AB The invention concerns the areas of immunol., mol. biol. and oncol. The aim of the invention is to improve immune reactions to viruses, tumors, auto-reactive proteins and cells such as autoantibodies, autoantigen-specific T-cell receptors (TCR) of auto-reactive T-cells, autoantigen-specific B-cell-receptors (BCR) of auto-reactive B-lymphocytes and autoantigen-specific MHC of the "unprofessional" antigen-presenting cells (APC). The **fusion** proteins can contain histidine tags and/or glycine tags and/or tyrosine or serine tags for phosphorylation by kinases. For example, **fusion** proteins for improving immune responses to B-cell tumors may contain **Fc** regions fused to CD5, CD28, or CTLA-4.

L11 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

2002:849789 Document No. 137:368556 Chimeric proteins comprising IgG inhibitory receptor-binding epitope and IgE receptor-binding epitope for treating allergies and other immune diseases. Saxon, Andrew; Zhang, Ke; Zhu, Daocheng (Regents of the University of California, USA). PCT Int. Appl. WO 2002088317 A2 20021107, 116 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US13527 20020501. PRIORITY: US 2001-2001/847208 20010501; US 2001-2001/439 20011024.

AB The invention concerns bifunctional **fusion** mols., and novel, safer and more efficacious methods for the treatment of immune disorders resulting from excessive or unwanted immune responses. The invention provides methods for the suppression of type I hypersensitive (i.e., IgE-mediated) allergic conditions, methods for the prevention of anaphylactic responses that occur as a result of traditional peptide immunotherapies for allergic and autoimmune disorders, and provides novel methods for the treatment of autoimmune conditions, where the methods have reduced risk of triggering an anaphylactic response. The invention provides novel therapeutic approaches for the treatment of allergic responses, including the prevention of anaphylactic response that can occur from environmental allergen exposure. The invention also provides methods for the treatment of autoimmune disorders such as multiple sclerosis, autoimmune type I diabetes mellitus, and rheumatoid arthritis. The invention also provides methods for preventing anaphylactic response during traditional antigen therapies.

L11 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

2002:157819 Document No. 136:215393 Chimeric protein comprising autoantigen domain and effector molecule for elimination of autoreactive B-cells. Zocher, Marcel; Baeuerle, Patrick; Dreier, Torsten (Micromet A.-G., Germany). PCT Int. Appl. WO 2002016414 A2 20020228, 96 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-EP9714 20010822. PRIORITY: EP 2000-117354 20000822.

AB The present invention relates to a composition for the selective elimination of autoreactive B-cells comprising at least one (poly)peptide construct consisting of at least two domains wherein one of said domains comprises an autoreactive antigen or (a) fragments(s) thereof specifically recognized by the Ig. receptors of said autoreactive B-cells and wherein one of said domains comprises an effector mol. capable of interacting with

and/or of activating NK-cells, T-cells, macrophages, monocytes and/or granulocytes and/or capable of activating the complement system. Thus, **fusion** proteins comprising myelin oligodendrocyte glycoprotein (MOG) and CD3 or human IgG1 **Fc** fragment were prepared and tested for removal of autoreactive B cells.

L11 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
2002:256739 Document No. 136:273217 Methods for promoting production of myelin by Schwann cells and treating demyelinating diseases using Zcyto7 or IL-17. Moore, Emma E.; Novak, Julia E. (USA). U.S. Pat. Appl. Publ. US 2002039568 A1 20020404, 21 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-794705 20010227. PRIORITY: US 2000-2000/PV185666 20000229.
AB A method for promoting the expression of myelin or Protein Zero in Schwann cells using Zcyto7 or IL-17 is described. Zcyto7 or IL-17 are further used to promote myelination of the peripheral nervous system. This is particularly useful in treating demyelinating diseases such as diabetic neuropathy, Guillain-Barre Syndrome, chronic demyelinating disease, acute demyelinating polyneuropathy and human immunodeficiency viral demyelinating neuropathy or demyelination caused by trauma. Human Zcyto7 at 100 ng/mL induced the expression of protein zero by primary rat Schwann cells.

L11 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
2002:241369 Document No. 136:261819 Coupling of peripheral tolerance to endogenous IL-10 promotes effective modulation of T cells and ameliorates autoimmune disease. Zaghouani, Habib (USA). U.S. Pat. Appl. Publ. US 2002038002 A1 20020328, 84 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-873901 20010604. PRIORITY: US 2000-2000/PV209527 20000605.
AB Immunomodulating agents comprising at least one **Fc** receptor ligand and at least one immunosuppressive factor are provided as are methods for their manufacture and use. The immunomodulating agents may be in the form of polypeptides or chimeric antibodies and preferably incorporate an immunosuppressive factor comprising a T cell receptor agonist or antagonist. The compds. and compns. of the invention may be used to selectively suppress the immune system to treat symptoms associated with immune disorders such as allergies, transplanted tissue rejection and autoimmune disorders including autoimmune diabetes, rheumatoid arthritis and multiple sclerosis.

L11 ANSWER 12 OF 23 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
2002:290043 The Genuine Article (R) Number: 534MV. A non-class I MHC intestinal epithelial surface glycoprotein, gp180, binds to CD8. Campbell N A (Reprint); Park M S; Toy L S; Yio X Y; Devine L; Kavathas P; Mayer L. Mt Sinai Med Ctr, Div Clin Immunol, New York, NY 10029 USA (Reprint); Yale Univ, Dept Lab Med, New Haven, CT 06511 USA. CLINICAL IMMUNOLOGY (MAR 2002) Vol. 102, No. 3, pp. 267-274. ISSN: 1521-6616. Publisher: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The activation of CD8(+) T cells by normal intestinal epithelial cells in antigen-specific or allogeneic mixed cell culture systems has significant implications for the modulation of mucosal immune responses due to the fact that these T cells appear to have regulatory rather than cytolytic activity. A 180-kDa glycoprotein (gp180) has been identified and shown to be important in CD8(+) T cell activation by intestinal epithelial cells. In this study, we examine, in further detail, the role that the CD8 molecule plays in this interaction. It has been previously shown that monoclonal antibodies against gp180 inhibited the activation of CD8-associated P56(lck) in T cells. Although indirectly suggested by these data, there was no evidence that the activation of this protein tyrosine kinase was a direct result of gp180 interacting with the CD8 molecule. In this study, we document that soluble gp180 is able to bind to CD8-**Fc fusion** proteins and is absorbed by human

CD8alpha but not CD4 transfected murine T cells and that this interaction is dependent upon carbohydrate on the gp180 molecule. Furthermore, the sites used for binding by gp180 are distinct from those used by the conventional CD8 ligand, class I MHC. Thus, gp180 appears to be a novel CD8 ligand that plays an important role in the activation of CD8-associated kinases and of CD8(+) T cells. (C) 2002 Elsevier Science (USA).

L11 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
2003:468095 Document No. 139:357756 Chimeric proteins: A novel approach for eliminating specific cell populations for targeted human therapy. Ben-Yehudah, Ahmi; Belostotsky, Ruth; Aqeilan, Rami; Azar, Yehudith; Steinberger, Ida; Fishman, Ala; Nechushtan, Amotz; Yarkoni, Shai; Lorberboum-Galski, Haya (Department of Cellular Biochemistry and Human Genetics, Hebrew University-Hadassah Medical School, Jerusalem, 91120, Israel). Cellular and Molecular Mechanisms of Toxin Action, Volume 4, 148-167. Editor(s): Lazarovici, Philip. Taylor & Francis Ltd.: London, UK. (English) 2002. CODEN: 64JPAO.
AB A review. One of the most widely used toxins in chimeric proteins is the bacterial toxin Pseudomonas exotoxin (PE) produced by the bacterium Pseudomonas aeruginosa. Various chimeric proteins were constructed using two modified forms of the PE toxin: (a) in which Domain I is deleted, generating the PE40 truncated form of PE, (b) by introducing mutations into the binding domain (Domain I) of PE (at amino acid positions 57, 246, 247, 249, all substituted by Glu) to generate the PE664GOu mutated form of PE. The authors designed a number of chimeric proteins for the cure of unrelated disorders: autoimmune diseases, allergy and cancer. For each of these diseases the authors constructed chimeric proteins carrying a specific targeting moiety: Interleukin-2 (IL2) for eliminating activated T cells involved in many human diseases, **myelin basic protein** (MBP) for therapy of multiple sclerosis (MS), **Fc** ε for use in the treatment of asthma and other allergic disorders and gonadotropin releasing hormone (GnRH) for targeting adenocarcinomas.

L11 ANSWER 14 OF 23 MEDLINE on STN
2001364658. PubMed ID: 11418697. A retro-inverso peptide mimic of CD28 encompassing the MYPPPY motif adopts a polyproline type II helix and inhibits encephalitogenic T cells in vitro. Srinivasan M; Wardrop R M; Gienapp I E; Stuckman S S; Whitacre C C; Kaumaya P T. (Department of Microbiology, College of Biological Sciences, Ohio State University, Columbus, OH 43210, USA.) Journal of immunology (Baltimore, Md. : 1950), (2001 Jul 1) Vol. 167, No. 1, pp. 578-85. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
AB Complete activation of T cells requires two signals: an Ag-specific signal delivered via the TCR by the peptide-MHC complex and a second costimulatory signal largely provided by B7:CD28/CTLA-4 interactions. Previous studies have shown that B7 blockade can either ameliorate experimental autoimmune encephalomyelitis by interfering with CD28 signaling or exacerbate the disease by concomitant blockade of CTLA-4 interaction. Therefore, we developed a functional CD28 mimic to selectively block B7:CD28 interactions. The design, synthesis, and structural and functional properties of the CD28 free peptide, the end group-blocked CD28 peptide, and its retro-inverso isomer are shown. The synthetic T cell-costimulatory receptor peptides fold into a polyproline type II helical structure commonly seen in regions of globular proteins involved in transient protein-protein interactions. The binding determinants of CD28 can be transferred onto a short peptide mimic of its ligand-binding region. The CD28 peptide mimics effectively block the expansion of encephalitogenic T cells in vitro suggesting the potential usefulness of the peptides for the treatment of autoimmune disease conditions requiring down-regulation of T cell responses.

L11 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
2000:34907 Document No. 132:92309 Compounds, compositions and methods for the endocytic presentation of immunosuppressive factors. Zaghouani, Habib

(The University of Tennessee Research Corporation, USA). PCT Int. Appl. WO 2000001732 A2 20000113, 80 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US15225 19990706. PRIORITY: US 1998-111123 19980706.

AB A **fusion** protein for the alleviation of symptoms associated with an autoimmune disorder comprising an Ig or portion thereof linked to one or more autoantigenic polypeptides or fragments thereof, wherein said Ig or portion thereof is capable of binding to an **Fc** receptor and being endocytosed by an antigen-presenting cell, and said one or more autoantigenic polypeptides or fragments thereof provides more than one T cell receptor peptide agonist for presentation on the surface of said antigen-presenting cell upon endocytic processing. Said autoantigenic polypeptides may comprise at least a portion of **myelin basic protein** or at least a portion of proteolipid protein. Method to alleviate symptoms associated with an autoimmune disorder in a patient in need thereof comprising the steps of providing a composition comprising said **fusion** protein and administering a therapeutically effective amount of said composition to said patient. Autoimmune disorders may include multiple sclerosis, lupus, rheumatoid arthritis, scleroderma, insulin-dependent diabetes and ulcerative colitis. Method for presenting multiple T cell receptor agonists on the surface of a professional or nonprofessional antigen-presenting cell comprising the steps of providing said **fusion** protein, contacting said **fusion** protein with at least one **Fc** receptor present on the surface of a professional or nonprofessional antigen-presenting cell, whereby the **fusion** protein is internalized by the antigen-presenting cell, and endocytically processing the internalized **fusion** protein to provide more than one T cell receptor peptide agonist, wherein the provided T cell receptor agonists are presented on the surface of the antigen-presenting cell.

L11 ANSWER 16 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

2000:323738 Document No.: PREV200000323738. Kinetics of T-cell receptor binding by bivalent HLA-DRcntdotpeptide complexes that activate antigen-specific human T-cells. Appel, Heiner; Gauthier, Laurent; Pyrdol, Jason; Wucherpfennig, Kai W. [Reprint author]. Dept. of Cancer Immunology and AIDS, Dana-Farber Cancer Institute, Boston, MA, 02115, USA. Journal of Biological Chemistry, (January 7, 2000) Vol. 275, No. 1, pp. 312-321. print.
CODEN: JBCHA3. ISSN: 0021-9258. Language: English.

AB Monovalent major histocompatibility complex-peptide complexes dissociate within seconds from the T-cell receptor (TCR), indicating that dimerization/multimerization may be important during early stages of T-cell activation. Soluble bivalent HLA-DR2cntdotmyelin basic protein (MBP) peptide complexes were expressed by replacing the F(ab) arms of an IgG2a antibody with HLA-DR2cntdotMBP peptide complexes. The binding of bivalent HLA-DR2cntdotpeptide complexes to recombinant TCR was examined by surface plasmon resonance. The bivalent nature greatly enhanced TCR binding and slowed dissociation from the TCR, with a t1/2 of 2.1 to 4.6 min. Soluble bivalent HLA-DR2cntdotMBP peptide complexes activated antigen-specific T-cells in the absence of antigen presenting cells. In contrast, soluble antibodies to the TCRcntdotCD3 complex were ineffective, indicating that they failed to induce an active TCR dimer. TCR/CD3 antibodies induced T-cell proliferation when bound by antigen presenting cells that expressed **Fc** receptors. In the presence of dendritic cells, bivalent HLA-DR2cntdotMBP peptide complexes induced T-cell activation at >100-fold lower concentrations than TCR/CD3 antibodies and

were also superior to peptide or antigen. These results demonstrate that bivalent HLA-DRcntdotpeptide complexes represent effective ligands for activation of the TCR. The data support a role for TCR dimerization in early TCR signaling and kinetic proofreading.

L11 ANSWER 17 OF 23 MEDLINE on STN DUPLICATE 3
2000279904. PubMed ID: 10818225. The in vitro activity of ADAM-10 is inhibited by TIMP-1 and TIMP-3. Amour A; Knight C G; Webster A; Slocombe P M; Stephens P E; Knauper V; Docherty A J; Murphy G. (School of Biological Sciences, University of East Anglia, Norwich, UK.) FEBS letters, (2000 May 19) Vol. 473, No. 3, pp. 275-9. Journal code: 0155157. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.
AB A recombinant soluble form of the catalytic domain of human ADAM-10 was expressed as an **Fc fusion** protein from myeloma cells. The ADAM-10 was catalytically active, cleaving **myelin basic protein** and peptides based on the previously described 'metallosheddase' cleavage sites of tumour necrosis factor alpha, CD40 ligand and amyloid precursor protein. The **myelin basic protein** degradation assay was used to demonstrate that hydroxamate inhibitors of matrix metalloproteinases (MMPs) were also inhibitors of ADAM-10. The natural MMP inhibitors, TIMP-2 and TIMP-4 were unable to inhibit ADAM-10, but TIMP-1 and TIMP-3 were inhibitory. Using a quenched fluorescent substrate assay and ADAM-10 we obtained approximate apparent inhibition constants of 0.1 nM (TIMP-1) and 0.9 nM (TIMP-3). The TIMP-1 inhibition of ADAM-10 could therefore prove useful in distinguishing its activity from that of TACE, which is only inhibited by TIMP-3, in cell based assays.

L11 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
1999:549393 Document No. 131:183867 Monovalent, multivalent, and multimeric MHC binding domain **fusion** proteins and conjugates, and uses therefor. Wucherpfennig, Kai W.; Strominger, Jack L. (President and Fellows of Harvard College, USA). PCT Int. Appl. WO 9942597 A1 19990826, 113 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US3603 19990219. PRIORITY: US 1998-PV75351 19980219.
AB The present invention is directed to the design, production, and use of monovalent, multivalent and multimeric major histocompatibility complex binding domain **fusion** proteins and conjugates. The MHC **fusion** proteins and conjugates may comprise MHC class II α or β chain (HLA-DRA*0101, HLA-DRA*0102, HLA-DQA1*0301, HLA-DRB1*01, etc.), leucine zipper domain of Fos or Jun, linker peptide, yeast σ-mating factor secretion signal, human **myelin basic protein** tag, IgG or IgE or IgM **Fc**, and optionally cytotoxic substance (human desmoglein 3 protein peptide). The MHC binding domain **fusion** proteins and conjugates are useful for diagnosis and treatment of diseases associated with T cell-mediated immune response and antigen presentation, e.g. autoimmune disease, multiple sclerosis and rheumatoid arthritis. Thus, **fusion** proteins containing HLA-DR2 α chain (β chain), Fos (Jun) leucine zipper dimerization domain, VDGGGGG linker, and α-mating secretion signal were prepared, fused with IgG2a or IgM, tagged with MBP peptide, conjugated with bead carrier, and used for selectively depletion of T cells.

L11 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
2000:186966 Document No. 133:176116 A gene therapy or purified CTLA4IgG treatment of experimental allergic encephalomyelitis. Kawaguchi, Yoshinori (Section of Immunopathogenesis, Institute of Immunological Science, Hokkaido University, Sapporo, 060-0815, Japan). Hokkaido Igaku

Zasshi, 74(6), 467-475 (English) 1999. CODEN: HOIZAK. ISSN: 0367-6102. Publisher: Hokkaido Igakkai.

AB We examined whether multiple i.p. injection of a soluble form of a chimeric protein consisting of an extracellular portion of cytotoxic T lymphocyte-associated protein 4 and an **Fc** portion of human IgG1(CTLA4IgG) at the initiation phase could successfully control the subsequent development of exptl. allergic encephalomyelitis (EAE). We demonstrated that CTLA4IgG treatment could delay the onset and reduce the severity of EAE in early phase of disease development. More importantly, CTLA4IgG treatment significantly reduced the incidence of EAE. This was in good agreement to that spleen cells obtained from CTLA4IgG-treated animals responded poorly to **myelin basic protein** (MBP) in vitro as compared to those from human IgG-treated animals. However, the CTLA4IgG-treated mice eventually developed EAE and after all, incidence of EAE was not significantly different from that in control group. We then tested whether a gene therapy using adenovirus vector containing CTLA4IgG (Adex1CACTLA4IgG) could inhibit the development of EAE. We demonstrated that incidence and severity of EAE were significantly inhibited by a single injection of i.v. Adex1CACTLA4IgG up to 8 mo. Thus, this study demonstrated the efficacy of a single dose of adenovirus-mediated gene therapy in controlling EAE as compared to repeated injection of purified CTLA4IgG proteins.

L11 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

1998:285095 Document No. 129:66611 Vaccination with DNA encoding an immunodominant **myelin basic protein** peptide targeted to **Fc** of immunoglobulin G suppresses experimental autoimmune encephalomyelitis. Lobell, Anna; Weissert, Robert; Storch, Maria K.; Svanholm, Cecilia; De Graaf, Katrien L.; Lassmann, Hans; Andersson, Roland; Olsson, Tomas; Wigzell, Hans (Microbiology and Tumorbiology Center, Karolinska Institute, Stockholm, S-171 77, Swed.). Journal of Experimental Medicine, 187(9), 1543-1548 (English) 1998. CODEN: JEMEAV. ISSN: 0022-1007. Publisher: Rockefeller University Press.

AB The authors explore here if vaccination with DNA encoding an autoantigenic peptide can suppress autoimmune disease. For this purpose the authors used exptl. autoimmune encephalomyelitis (EAE), which is an autoaggressive disease in the central nervous system and an animal model for multiple sclerosis. Lewis rats were vaccinated with DNA encoding an encephalitogenic T cell epitope, guinea pig **myelin basic protein** peptide 68-85 (MBP68-85), before induction of EAE with MBP68-85 in complete Freund's adjuvant. Compared to vaccination with a control DNA construct, the vaccination suppressed clin. and histopathol. signs of EAE, and reduced the interferon γ production after challenge with MBP68-85. Targeting of the gene product to **Fc** of IgG was essential for this effect. There were no signs of a Th2 cytokine bias. The data suggest that DNA vaccines encoding autoantigenic peptides may be useful tools in controlling autoimmune disease.

L11 ANSWER 21 OF 23 MEDLINE on STN

1998230504. PubMed ID: 9570577. Expansion of autoreactive T cells in multiple sclerosis is independent of exogenous B7 costimulation. Scholz C; Patton K T; Anderson D E; Freeman G J; Hafler D A. (Laboratory of Molecular Immunology, Department of Neurology, Brigham and Women's Hospital, Boston, MA 02115, USA.) Journal of immunology (Baltimore, Md. : 1950), (1998 Feb 1) Vol. 160, No. 3, pp. 1532-8. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Multiple sclerosis (MS) is an inflammatory disease of the myelinated central nervous system that is postulated to be induced by myelin-reactive CD4 T cells. T cell activation requires an antigen-specific signal through the TCR and a costimulatory signal, which can be mediated by B7-1 or B7-2 engagement of CD28. To directly examine the activation state of myelin-reactive T cells in MS, the costimulation requirements necessary to activate **myelin basic protein** (MBP) or tetanus toxoid (TT)-reactive CD4 T cells were compared between normal controls and MS patients. Peripheral blood T cells were stimulated with

Chinese hamster ovary (CHO) cells transfected either with DRB1*1501/DRA0101 chains (t-DR2) alone, or in combination with, B7-1 or B7-2. In the absence of costimulation, T cells from normal subjects stimulated with the recall antigen TT p830-843 were induced to expand and proliferate, but stimulation with MBP p85-99 did not have this effect. In marked contrast, T cells from patients with MS stimulated with MBP p85-99 in the absence of B7-1 or B7-2 signals expanded and proliferated. Thus, MBP-reactive CD4 T cells in patients with MS are costimulation independent and have been previously activated in vivo. These experiments provide further direct evidence for a role of activated MBP-specific CD4 T cells in the pathogenesis of MS.

L11 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

1996:352596 Document No. 125:31803 Inhibition by CTLA4Ig of experimental allergic encephalomyelitis. Arima, Takeshi; Rehman, Atiq; Hickey, William F.; Flye, M. Wayne (Dep. Surg., Washington Univ. Sch. Med., St. Louis, MO, 63110, USA). Journal of Immunology, 156(12), 4916-4924 (English) 1996. CODEN: JOIMA3. ISSN: 0022-1767. Publisher: American Association of Immunologists.

AB B7-1 and B7-2 are well characterized costimulatory ligands on Ag presentation cells for the CD28 and CTLA4 receptors on T cells. The **fusion** protein CTLA4Ig can block this interaction and prevent specific T cell activation. The development of fatal CD4+ T cell-mediated exptl. allergic encephalomyelitis (EAE) in susceptible female Lewis rats was optimized by immunization with 20 mg of guinea pig spinal cord homogenate in CFA on day 0 with three doses of 1 μg pertussis toxin given i.v. on days 0, 3, and 7. This immunization regimen uniformly resulted in the development of severe clin. neurol. signs of EAE with 100% mortality by day 17 postimmunization. Treatment with 0.5 mg/dose of rhCTLA4-Ig on days -2, 0, 3, 6, 9, 12, 15, and 18 significantly decreased the incidence, delayed the onset, and reduced the severity of clin. EAE ($p = 0.0002$ vs control by the Mann-Whitney U test) enough to completely prevent fatal EAE, whereas treatment with control human IgG had no effect. Histol., perivascular neutrophilic infiltrates were also dramatically decreased in the spinal cords of animals treated with CTLA4 but not in those treated with control human IgG. The proliferative response to encephalitogenic Ags (guinea pig **myelin basic protein** and proteolipid protein) by lymph node cells from animals immunized with guinea pig spinal cord 10 days before was also significantly suppressed in vitro by CTLA4Ig (1 μg/mL). However, the protective effect of CTLA4Ig could be completely prevented by the daily i.p. administration, from day 0 to 10, of exogenous human rIL-2 (180,000 IU). These results indicate a critical requirement of the costimulatory B7/CD28 pathway early in the development of CD4+ T cell-mediated EAE in the rat.

L11 ANSWER 23 OF 23 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

1995:380552 The Genuine Article (R) Number: RB212. LONG-TERM INHIBITION OF MURINE EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS USING CTLA-4-**FC** SUPPORTS A KEY ROLE FOR CD28 COSTIMULATION. CROSS A H (Reprint); GIRARD T J; GIACOLETTO K S; EVANS R J; KEELING R M; LIN R F; TROTTER J L; KARR R W. WASHINGTON UNIV, SCH MED, DEPT NEUROL & NEUROSURG, ST LOUIS, MO 63110; GD SEARLE & CO, DEPT IMMUNOL, ST LOUIS, MO 63198. JOURNAL OF CLINICAL INVESTIGATION (JUN 1995) Vol. 95, No. 6, pp. 2783-2789. ISSN: 0021-9738. Publisher: ROCKEFELLER UNIV PRESS, 222 E 70TH STREET, NEW YORK, NY 10021. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB T cell activation involves not only recognition of antigen presented by the MHC, but also nonspecific interactions termed ''costimulation.'' The costimulatory molecules B7-1 and B7-2 are ligands on antigen-presenting cells for the CD28 and CTLA-4 receptors on T cells. Previously, a **fusion** protein consisting of human CTLA-4 linked to human **Fc** was shown to bind B7-1 and B7-2 with high avidity and to prevent specific T cell activation. Here we investigated the

effects of a recombinant **fusion** protein consisting of the extracellular domain of human CTLA-4 bound to mouse IgG2a **Fc** (CTLA-4-**Fc**) upon experimental autoimmune encephalomyelitis, a T cell-mediated disease that serves as a model for multiple sclerosis. CTLA-4-**Fc** prevented experimental autoimmune encephalomyelitis in 26 of 28 CTLA-4-**Fc**-treated mice (median maximum score 0), whereas 28 of 30 mice treated with control mouse IgG2a developed disease (median maximum score 2.75). Less inflammation and virtually no demyelination or axonal loss occurred in CTLA-4-**Fc**-treated compared with control-treated mice, Activated splenocytes from CTLA-4-**Fc**-treated mice were able to transfer disease adoptively to naive recipients. These results indicate a key role for the B7/CD28 system in the development of actively induced murine experimental autoimmune encephalomyelitis, suggesting an area of investigation with therapeutic potential for multiple sclerosis.

=> s l9 and IgG1
L12 13 L9 AND IGG1

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PROCESSING COMPLETED FOR L12
L13 11 DUP REMOVE L12 (2 DUPLICATES REMOVED)

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L13 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
2006:13021 Document No. 144:101055 Protein Sp35/LINGO-1 antagonists for treatment of conditions involving demyelination. Mi, Sha; Pepinsky, R. Blake; McCoy, John (Biogen Idec Ma Inc., USA). PCT Int. Appl. WO 2006002437 A2 20060105, 183 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-US22881 20050624. PRIORITY: US 2004-2004/PV58296U 20040624; US 2004-2004/PV61729U 20041007; US 2004-2004/PV62843U 20041115; US 2005-2005/PV680475 20050513.

AB The invention provides methods of treating diseases, disorders or injuries involving demyelination and dysmyelination, including multiple sclerosis, by the administration of an Sp35/LINGO-1 antagonist. The Sp35/LINGO-1 antagonists include soluble Sp35 peptides, Sp35 **fusion** products with antibodies or antibody fragments, and Sp35 antisense polynucleotides, ribozymes, siRNA, or small hairpin RNA. The invention further claims polypeptide sequences for human Sp35 polypeptide and peptides, and a DNA sequence for an Sp35 shRNA. The human Sp35 protein contains signal sequence, a domain with 14 leucine-rich repeats, an Ig domain, a transmembrane region, and a cytoplasmic domain. The human Sp35 gene contains alternative translation start codons, so that 6 addnl. amino acids may or may not be present at the N-terminus of the Sp35 signal sequence. Rat oligodendrocyte precursor cells were infected with a lentiviral vector containing Sp35/LINGO-1 RNAi. Endogenous Sp35 expression was reduced as determined by RT-PCR and this resulted in more highly differentiated, mature oligodendrocytes compared with the control. An Sp35-Fc **fusion** protein was constructed using the extracellular region of human Sp35 and human **IgG1** Fc region. Purified recombinant Sp35-Fc protein promoted differentiation of rat precursor cells into O4-expressing mature oligodendrocytes and increased the in vitro survival rate for MBP-expressing mature oligodendrocytes. Sp35-Fc **fusion** protein and Ig domain peptides of Sp35 promoted myelination in vitro in co-cultures of rat dorsal root ganglion neurons and oligodendrocytes. In vivo transplantation of Sp35-transformed cells to

injured rat spinal cords resulted in more oligodendrocyte and axon myelination and less axon retraction than in the control.

L13 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
2004:292071 Document No. 140:320040 36Fusion proteins comprising CD1d complex, α2 microglobulin and antibody or fragment for targeting therapy of tumor, autoimmune disease, inflammation and infection. Robert, Bruno; Donda, Alena; Cesson, Valerie; Mach, Jean-Pierre; Zauderer, Maurice (Vaccinex, Inc., USA). PCT Int. Appl. WO 2004029206 A2 20040408, 152 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US30238 20030926. PRIORITY: EP 2002-405838 20020927.
AB The invention is directed to a compound comprising one or more CD1d complexes in association with an antibody specific for a cell surface marker. The CD1d complexes comprise a CD1d, a ss2-microglobulin mol., and may further comprise an antigen bound to the CD1d binding groove. The invention is further directed to methods of inhibiting or stimulating an immune response with the CD1d-antibody compds., in particular anti-tumor and autoimmunity responses.

L13 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
2003:260853 Document No. 138:285999 Chimeric proteins comprising ITIM motif, antigen and FcεR binding peptide for treating immune diseases. Saxon, Andrew (USA). U.S. Pat. Appl. Publ. US 2003064063 A1 20030403, 51 pp., Cont.-in-part of U.S. Ser. No. 847,208. (English). CODEN: USXXCO. APPLICATION: US 2001-439 20011024. PRIORITY: US 2001-2001/847208 20010501.
AB The invention concerns bifunctional **fusion** mols., and novel, safer and more efficacious methods for the treatment of immune disorders resulting from excessive or unwanted immune responses. The invention provides methods for the suppression of type I hypersensitive (i.e., IgE-mediated) allergic conditions, methods for the prevention of anaphylactic responses that occur as a result of traditional peptide immunotherapies for allergic and autoimmune disorders, and provides novel methods for the treatment of autoimmune conditions, where the methods have reduced risk of triggering an anaphylactic response. The invention provides novel therapeutic approaches for the treatment of allergic responses, including the prevention of anaphylactic response that can occur from environmental allergen exposure. The invention also provides methods for the treatment of autoimmune disorders such as multiple sclerosis, autoimmune type I diabetes mellitus, and rheumatoid arthritis. The invention also provides methods for preventing anaphylactic response during traditional antigen therapies.

L13 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
2002:849789 Document No. 137:368556 Chimeric proteins comprising IgG inhibitory receptor-binding epitope and IgE receptor-binding epitope for treating allergies and other immune diseases. Saxon, Andrew; Zhang, Ke; Zhu, Daocheng (Regents of the University of California, USA). PCT Int. Appl. WO 2002088317 A2 20021107, 116 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US13527 20020501. PRIORITY: US 2001-2001/847208 20010501; US

2001-2001/439 20011024.

AB The invention concerns bifunctional **fusion** mols., and novel, safer and more efficacious methods for the treatment of immune disorders resulting from excessive or unwanted immune responses. The invention provides methods for the suppression of type I hypersensitive (i.e., IgE-mediated) allergic conditions, methods for the prevention of anaphylactic responses that occur as a result of traditional peptide immunotherapies for allergic and autoimmune disorders, and provides novel methods for the treatment of autoimmune conditions, where the methods have reduced risk of triggering an anaphylactic response. The invention provides novel therapeutic approaches for the treatment of allergic responses, including the prevention of anaphylactic response that can occur from environmental allergen exposure. The invention also provides methods for the treatment of autoimmune disorders such as multiple sclerosis, autoimmune type I diabetes mellitus, and rheumatoid arthritis. The invention also provides methods for preventing anaphylactic response during traditional antigen therapies.

L13 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

2002:157819 Document No. 136:215393 Chimeric protein comprising autoantigen domain and effector molecule for elimination of autoreactive B-cells. Zocher, Marcel; Baeuerle, Patrick; Dreier, Torsten (Micromet A.-G., Germany). PCT Int. Appl. WO 2002016414 A2 20020228, 96 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-EP9714 20010822. PRIORITY: EP 2000-117354 20000822.

AB The present invention relates to a composition for the selective elimination of autoreactive B-cells comprising at least one (poly)peptide construct consisting of at least two domains wherein one of said domains comprises an autoreactive antigen or (a) fragments(s) thereof specifically recognized by the Ig. receptors of said autoreactive B-cells and wherein one of said domains comprises an effector mol. capable of interacting with and/or of activating NK-cells, T-cells, macrophages, monocytes and/or granulocytes and/or capable of activating the complement system. Thus, **fusion** proteins comprising myelin oligodendrocyte glycoprotein (MOG) and CD3 or human **IgG1** Fc fragment were prepared and tested for removal of autoreactive B cells.

L13 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

2002:107078 Document No. 136:166050 Novel methods and compositions to upregulate, redirect or limit immune responses to peptides, proteins and other bioactive compounds and vectors expressing the same. Bot, Adrian; Dellamary, Luis; Smith, Dan J.; Woods, Catherine M. (Alliance Pharmaceutical Corp., USA). PCT Int. Appl. WO 2002009674 A2 20020207, 80 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US24038 20010730. PRIORITY: US 2000-2000/PV221544 20000728.

AB Novel compns. are disclosed which can induce or enhance an immune response against foreign or self antigens (microbial or parasitic) or modulate (suppress) the activity of pathogenic cells in inflammatory or autoimmune diseases. Compns. and methods are taught in how to limit the generation of an immune response against formulated peptides and proteins with

application in antibody therapy or hormone replacement therapy. Methods of suppressing autoimmunity are also disclosed which use ligands for cellular receptors expressed on cells of the innate immune system and more specifically for down-regulation of autoimmune processes by either deletion or induction of anergy at the level of autoreactive T cells or by triggering active-suppressor T cells that down-regulate the activity of pathogenic cells.

L13 ANSWER 7 OF 11 MEDLINE on STN DUPLICATE 1

1999394501. PubMed ID: 10466625. Prevention of experimental allergic encephalomyelitis by intramuscular gene transfer with cytokine-encoding plasmid vectors. Piccirillo C A; Prud'homme G J. (Department of Pathology and Center for Clinical Immunobiology and Transplantation, McGill University, Montreal, Quebec, Canada.) Human gene therapy, (1999 Aug 10) Vol. 10, No. 12, pp. 1915-22. Journal code: 9008950. ISSN: 1043-0342. Pub. country: United States. Language: English.

AB Antiinflammatory cytokines such as transforming growth factor beta1 (TGF-beta1) and interleukin 4 (IL-4) can protect from autoimmune diseases. To study the immunoregulatory effects of these cytokines in vivo, we used a method of gene therapy that permits continuous cytokine delivery over a period of weeks. We injected naked plasmid DNA expression vectors encoding either TGF-beta1 (pVR-TGF-beta1) or an IL-4-**IgG1** chimeric protein (pVR-IL-4-**IgG1**) intramuscularly. This resulted in production of TGF-beta1 or IL-4-**IgG1**, respectively, and protection from **myelin basic protein** (MBP)-induced experimental allergic encephalomyelitis (EAE). TGF-beta1 gene delivery had pronounced downregulatory effects on T cell proliferation and production of interferon gamma (IFN-gamma) and tumor necrosis factor alpha (TNF-alpha), on in vitro restimulation with MBP. IL-4-**IgG1** vector administration also suppressed these responses, although much less than TGF-beta1, and enhanced secretion of endogenous IL-4. Therapy resulted in a significant decrease in the severity of histopathologic inflammatory lesions. In the CNS, treatment with either vector suppressed IL-12 and IFN-gamma mRNA expression, while IL-4 and TGF-beta1 mRNA levels were increased compared with control mice. Thus, cytokine plasmid treatment appeared to inhibit MBP-specific pathogenic Th1 responses, while enhancing endogenous secretion of protective cytokines. We demonstrate that gene therapy with these vectors is an effective therapeutic strategy for EAE.

L13 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

2000:186966 Document No. 133:176116 A gene therapy or purified CTLA4IgG treatment of experimental allergic encephalomyelitis. Kawaguchi, Yoshinori (Section of Immunopathogenesis, Institute of Immunological Science, Hokkaido University, Sapporo, 060-0815, Japan). Hokkaido Igaku Zasshi, 74(6), 467-475 (English) 1999. CODEN: HOIZAK. ISSN: 0367-6102. Publisher: Hokkaido Igakkai.

AB We examined whether multiple i.p. injection of a soluble form of a chimeric protein consisting of an extracellular portion of cytotoxic T lymphocyte-associated protein 4 and an Fc portion of human **IgG1** (CTLA4IgG) at the initiation phase could successfully control the subsequent development of exptl. allergic encephalomyelitis (EAE). We demonstrated that CTLA4IgG treatment could delay the onset and reduce the severity of EAE in early phase of disease development. More importantly, CTLA4IgG treatment significantly reduced the incidence of EAE. This was in good agreement to that spleen cells obtained from CTLA4IgG-treated animals responded poorly to **myelin basic protein** (MBP) in vitro as compared to those from human IgG-treated animals. However, the CTLA4IgG-treated mice eventually developed EAE and after all, incidence of EAE was not significantly different from that in control group. We then tested whether a gene therapy using adenovirus vector containing CTLA4IgG (Adex1CACTLA4IgG) could inhibit the development of EAE. We demonstrated that incidence and severity of EAE were significantly inhibited by a single injection of i.v. Adex1CACTLA4IgG up to 8 mo. Thus, this study demonstrated the efficacy of a single dose of

adenovirus-mediated gene therapy in controlling EAE as compared to repeated injection of purified CTLA4IgG proteins.

L13 ANSWER 9 OF 11 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 2

97043333 EMBASE Document No.: 1997043333. TNF-α receptor **fusion** protein prevents experimental auto-immune encephalomyelitis and demyelination in Lewis rats: An overview. Klinkert W.E.F.; Kojima K.; Lesslauer W.; Rinner W.; Lassmann H.; Wekerle H.. W.E.F. Klinkert, Department of Neuroimmunology, Max-Planck Institute for Psychiatry, D-82152 Martinsried, Germany. klinkert@alf.biochem.mpg.de. Journal of Neuroimmunology Vol. 72, No. 2, pp. 163-168 1997.
Refs: 44.
ISSN: 0165-5728. CODEN: JNRIDW
S 0165-5728(96)00183-X. Pub. Country: Netherlands. Language: English. Summary Language: English.

ED Entered STN: 970324

AB To explore the therapeutic use of TNF-α inhibitors in human inflammatory demyelinating diseases we examined the effect of a recombinant TNFRp55 protein constructed by fusing TNFRp55 extracellular domain cDNA to a human **IgG1** heavy gene fragment containing the hinge and constant domains CH2 and CH3 (TNFRp55-**IgG1**) in diverse experimental model systems representing inflammation and inflammatory demyelination of encephalitogenic T cells in vivo. In EAE actively induced by immunization of Lewis rats with MBP, a single dose of TNFRp55-**IgG1** protected the recipient animals from clinical signs. Interestingly, the treatment neither prevented the formation CNS infiltrations, nor did it alter the cellar composition of the infiltrates. In EAE transferred by MBP specific activated T line cells, a model of inflammatory (not demyelinating) brain disease, the inhibitor's therapeutic effect on clinical disease was also striking achieving almost complete protection even after repeated transfers of encephalitogenic T cells. Finally, the recombinant inhibitor was also protective in Lewis rats with demyelinating experimental autoimmune panencephalitis produced by combined transfer of panencephalitogenic T cells and demyelinating monoclonal antibody specific for MOG. In this system, the T cells are of low encephalitogenic activity, but open the blood-brain barrier for the demyelinating immunoglobulins. The **fusion** protein treatment, however, prevented the formation of inflammatory lesions and demyelination. The strong therapeutic effect of the recombinant chimeric TNF-α inhibitor in three models of myelin specific autoimmunity raises hopes as to TNF-α directed therapy of human diseases like MS.

L13 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

1996:352596 Document No. 125:31803 Inhibition by CTLA4Ig of experimental allergic encephalomyelitis. Arima, Takeshi; Rehman, Atiq; Hickey, William F.; Flye, M. Wayne (Dep. Surg., Washington Univ. Sch. Med., St. Louis, MO, 63110, USA). Journal of Immunology, 156(12), 4916-4924 (English) 1996. CODEN: JOIMA3. ISSN: 0022-1767. Publisher: American Association of Immunologists.

AB B7-1 and B7-2 are well characterized costimulatory ligands on Ag presentation cells for the CD28 and CTLA4 receptors on T cells. The **fusion** protein CTLA4Ig can block this interaction and prevent specific T cell activation. The development of fatal CD4+ T cell-mediated exptl. allergic encephalomyelitis (EAE) in susceptible female Lewis rats was optimized by immunization with 20 mg of guinea pig spinal cord homogenate in CFA on day 0 with three doses of 1 μg pertussis toxin given i.v. on days 0, 3, and 7. This immunization regimen uniformly resulted in the development of severe clin. neurol. signs of EAE with 100% mortality by day 17 postimmunization. Treatment with 0.5 mg/dose of rhCTLA4-Ig on days -2, 0, 3, 6, 9, 12, 15, and 18 significantly decreased the incidence, delayed the onset, and reduced the severity of clin. EAE ($p = 0.0002$ vs control by the Mann-Whitney U test) enough to completely prevent fatal EAE, whereas treatment with control human IgG had no effect. Histol., perivascular neutrophilic infiltrates were also dramatically

decreased in the spinal cords of animals treated with CTLA4 but not in those treated with control human IgG. The proliferative response to encephalitogenic Ags (guinea pig **myelin basic protein** and proteolipid protein) by lymph node cells from animals immunized with guinea pig spinal cord 10 days before was also significantly suppressed in vitro by CTLA4Ig (1 μg/mL). However, the protective effect of CTLA4Ig could be completely prevented by the daily i.p. administration, from day 0 to 10, of exogenous human rIL-2 (180,000 IU). These results indicate a critical requirement of the costimulatory B7/CD28 pathway early in the development of CD4+ T cell-mediated EAE in the rat.

L13 ANSWER 11 OF 11 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

1995:284955 The Genuine Article (R) Number: QV929. CD28-B7 BLOCKADE AFTER ALLOANTIGENIC CHALLENGE IN-VIVO INHIBITS TH1 CYTOKINES BUT SPARES TH2. SAYEGH M H (Reprint); AKALIN E; HANCOCK W W; RUSSELL M E; CARPENTER C B; LINSLEY P S; TURKA L A. HARVARD UNIV, BRIGHAM & WOMENS HOSP, SCH MED, DEPT MED, DIV RENAL, IMMUNOGENET & TRANSPLANTAT LAB, BOSTON, MA 02115 (Reprint); HARVARD UNIV, NEW ENGLAND DEACONESS HOSP, SCH MED, DEPT PATHOL, BOSTON, MA 02115; HARVARD UNIV, SCH MED, SANDOZ CTR IMMUNOBIOL, BOSTON, MA 02115; HARVARD UNIV, SCH PUBL HLTH, BOSTON, MA 02115; HARVARD UNIV, BRIGHAM & WOMENS HOSP, SCH MED, BOSTON, MA 02115; BRISTOL MYERS SQUIBB PHARMACEUT RES INST, SEATTLE, WA 98121; UNIV PENN, DEPT INTERNAL MED, PHILADELPHIA, PA 19104; UNIV PENN, INST HUMAN GENE THERAPY, PHILADELPHIA, PA 19104. JOURNAL OF EXPERIMENTAL MEDICINE (1 MAY 1995) Vol. 181, No. 5, pp. 1869-1874. ISSN: 0022-1007. Publisher: ROCKEFELLER UNIV PRESS, 222 E 70TH STREET, NEW YORK, NY 10021. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Blocking the CD28-B7 T cell costimulatory pathway with the **fusion** protein CTLA4Ig inhibits alloimmune responses in vitro and in vivo and induces tolerance to cardiac allografts in mice and rats, but the mechanisms mediating the tolerant state in vivo are unknown. Here, we report the effects and potential mechanisms of CTLA4Ig in the rat renal allograft model. LEW rats were nephrectomized and received renal allografts from major histocompatibility complex-incompatible WF rats. While all untreated and control immunoglobulin (Ig)-treated animals acutely rejected their allografts and died, 86% of rats that received a single injection of CTLA4Ig on day 2 after transplantation had prolonged survival (>60-100 days) with preserved renal function. By contrast, only 29% of animals that received CTLA4Ig on the day of engraftment had prolonged survival. Long-term survivors (>100 days) exhibited donor-specific tolerance, accepting donor-matched WF but acutely rejecting third-party BN cardiac allografts. Immunohistological analysis of grafts sampled at 1 week after transplantation showed that both control and CTLA4Ig-treated animals had mononuclear cell infiltrates, with a higher percentage of CD4(+) cells in the CTLA4Ig-treated group. However, while this was associated with vasculitis and tubulitis in control grafts, there was no evidence of tissue injury in CTLA4Ig-treated animals. The immune response leading to graft rejection in control animals was characterized by expression of the T helper (Th) type 1 cytokines interleukin (IL)-2 and interferon-gamma. In contrast, the persistent CD4(+) infiltrate without graft rejection in CTLA4Ig-treated animals was associated with increased staining for the Th2-related cytokines IL-4 and IL-10. Furthermore, grafts from CTLA4Ig-treated animals had marked upregulation of intragraft staining for **IgG1**, but not IgG2a or IgG2b. Administration of rIL-2 to CTLA4Ig-treated animals restored allograft rejection in 50% of animals tested. These results confirm that blockade of the CD28-B7 pathway after alloantigenic challenge induces donor-specific acceptance of vascularized organ allografts, and indicates in this model that CTLA4Ig inhibits Th1 but spares Th2 cytokines in vivo.

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L15 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
2004:292071 Document No. 140:320040 36Fusion proteins comprising CD1d complex, α2 microglobulin and antibody or fragment for targeting therapy of tumor, autoimmune disease, inflammation and infection. Robert, Bruno; Donda, Alena; Cesson, Valerie; Mach, Jean-Pierre; Zauderer, Maurice (Vaccinex, Inc., USA). PCT Int. Appl. WO 2004029206 A2 20040408, 152 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US30238 20030926. PRIORITY: EP 2002-405838 20020927.
AB The invention is directed to a compound comprising one or more CD1d complexes in association with an antibody specific for a cell surface marker. The CD1d complexes comprise a CD1d, a ss2-microglobulin mol., and may further comprise an antigen bound to the CD1d binding groove. The invention is further directed to methods of inhibiting or stimulating an immune response with the CD1d-antibody compds., in particular anti-tumor and autoimmunity responses.

L15 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
2003:260853 Document No. 138:285999 Chimeric proteins comprising ITIM motif, antigen and FcεR binding peptide for treating immune diseases. Saxon, Andrew (USA). U.S. Pat. Appl. Publ. US 2003064063 A1 20030403, 51 pp., Cont.-in-part of U.S. Ser. No. 847,208. (English). CODEN: USXXCO. APPLICATION: US 2001-439 20011024. PRIORITY: US 2001-2001/847208 20010501.
AB The invention concerns bifunctional **fusion** mols., and novel, safer and more efficacious methods for the treatment of immune disorders resulting from excessive or unwanted immune responses. The invention provides methods for the suppression of type I hypersensitive (i.e., IgE-mediated) allergic conditions, methods for the prevention of anaphylactic responses that occur as a result of traditional peptide immunotherapies for allergic and autoimmune disorders, and provides novel methods for the treatment of autoimmune conditions, where the methods have reduced risk of triggering an anaphylactic response. The invention provides novel therapeutic approaches for the treatment of allergic responses, including the prevention of anaphylactic response that can occur from environmental allergen exposure. The invention also provides methods for the treatment of autoimmune disorders such as multiple sclerosis, autoimmune type I diabetes mellitus, and rheumatoid arthritis. The invention also provides methods for preventing anaphylactic response during traditional antigen therapies.

L15 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
2002:849789 Document No. 137:368556 Chimeric proteins comprising IgG inhibitory receptor-binding epitope and IgE receptor-binding epitope for treating allergies and other immune diseases. Saxon, Andrew; Zhang, Ke; Zhu, Daocheng (Regents of the University of California, USA). PCT Int. Appl. WO 2002088317 A2 20021107, 116 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN,

YU, ZA, ZM, ZW, AM, AZ, BY, KG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US13527 20020501. PRIORITY: US 2001-2001/847208 20010501; US 2001-2001/439 20011024.

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L15 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

2001:828415 Document No. 137:89412 Detection of variations in the DNA methylation profile of genes in the determining the risk of disease. Berlin, Kurt; Piepenbrock, Christian; Olek, Alexander (Epigenomics A.-G., Germany). PCT Int. Appl. WO 2001077373 A2 20011018, 636 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2001-XA1486 20010406. PRIORITY: DE 2000-10019058 20000406; WO 2001-DE1486 20010406.

AB The invention relates to an oligonucleotide kit as probe for the detection of relevant variations in the DNA methylation of a target group of genes. The invention further relates to the use of the same for determining the gene variant with regard to DNA methylation, a medical device, using an oligonucleotide kit, a method for determining the methylation state of an individual and a method for the establishment of a model for establishing the probability of onset of a disease state in an individual. Such diseases may be: undesired pharmaceutical side-effects; cancerous diseases; CNS dysfunctions, injuries or diseases; aggressive symptoms or relational disturbances; clin., psychol. and social consequences of brain injury; psychotic disorders and personality disorders; dementia and/or associated syndromes; cardiovascular disease, dysfunction and damage; dysfunction, damage or disease of the gastrointestinal tract; dysfunction, damage or disease of the respiratory system; injury, inflammation, infection, immunity and/or anastasis; dysfunction, damage or disease of the body as an abnormal development process; dysfunction, damage or disease of the skin, muscle, connective tissue or bones; endocrine and metabolic dysfunction, damage or disease; headaches or sexual dysfunction. This abstract record is one of several records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.

=> s l9 and IgG3
L16 8 L9 AND IGG3

=> dup remove l16
PROCESSING COMPLETED FOR L16
L17 4 DUP REMOVE L16 (4 DUPLICATES REMOVED)

=> d l17 1-4 cbib abs

L17 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
2004:292071 Document No. 140:320040 36Fusion proteins comprising CD1d complex, α2 microglobulin and antibody or fragment for targeting therapy of tumor, autoimmune disease, inflammation and infection. Robert, Bruno; Donda, Alena; Cesson, Valerie; Mach, Jean-Pierre; Zauderer, Maurice (Vaccinex, Inc., USA). PCT Int. Appl. WO 2004029206 A2 20040408, 152 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US30238 20030926. PRIORITY: EP 2002-405838 20020927.

AB The invention is directed to a compound comprising one or more CD1d complexes in association with an antibody specific for a cell surface marker. The CD1d complexes comprise a CD1d, a ss2-microglobulin mol., and may further comprise an antigen bound to the CD1d binding groove. The invention is further directed to methods of inhibiting or stimulating an immune response with the CD1d-antibody compds., in particular anti-tumor and autoimmunity responses.

L17 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 1
2004209928. PubMed ID: 14988414. NTB-A, a new activating receptor in T cells that regulates autoimmune disease. Valdez Patricia A; Wang Hua; Seshasayee Dhaya; van Lookeren Campagne Menno; Gurney Austin; Lee Wyne P; Grewal Iqbal S. (Department of Immunology and Molecular Biology, Genentech Inc., South San Francisco, California 94080, USA.) The Journal of biological chemistry, (2004 Apr 30) Vol. 279, No. 18, pp. 18662-9. Electronic Publication: 2004-02-26. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB The CD28 co-stimulatory pathway is well established for T cell activation; however, results from CD28 -/- mice suggest the existence of additional co-stimulatory pathways. Here we report the further characterization of a new member of the CD2 superfamily, NTB-A, important in T cell co-stimulation. NTB-A is expressed on T cells, and its expression is up-regulated on activated cells. Triggering of NTB-A with monoclonal antibodies in the absence of CD28 signals leads to T cell proliferation and interferon-gamma secretion but not interleukin-4. Cross-linking of NTB-A also induces phosphorylation of NTB-A and the association of SAP (SLAM-associated protein), the protein absent in X-linked lymphoproliferative disease. T helper cells differentiated by cross-linking NTB-A and CD3 developed predominantly into Th1 cells not Th2 cells. In vivo blocking of NTB-A interactions with its ligands by using soluble NTB-A-Fc **fusion** protein inhibits B cell isotype switching to IgG2a and **IgG3**, commonly induced by Th1-type cytokines. Most important, treatment of mice with NTB-A-Fc delays the onset of antigen-induced experimental allergic encephalomyelitis in **myelin basic protein**-T cell receptor transgenic mice, suggesting a role in T cell-mediated autoimmune disease. Regulation of interferon-gamma secretion, and not interleukin-4 in vitro, as well as inhibition of Th1 cell-induced isotype switching and attenuation of experimental allergic encephalomyelitis indicate that NTB-A is important for Th1 responses. The observation that cross-linking of NTB-A induces T cell activation, expansion, and Th1-type cytokine production suggests NTB-A is a novel co-stimulatory receptor. The identification of NTB-A as a regulator of T cell response paves the way to provide novel therapeutic approaches for modulation of the immune response.

L17 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

2003:260853 Document No. 138:285999 Chimeric proteins comprising ITIM motif, antigen and FcεR binding peptide for treating immune diseases. Saxon, Andrew (USA). U.S. Pat. Appl. Publ. US 2003064063 A1 20030403, 51 pp., Cont.-in-part of U.S. Ser. No. 847,208. (English). CODEN: USXXCO. APPLICATION: US 2001-439 20011024. PRIORITY: US 2001-2001/847208 20010501.

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L17 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

2002:849789 Document No. 137:368556 Chimeric proteins comprising IgG inhibitory receptor-binding epitope and IgE receptor-binding epitope for treating allergies and other immune diseases. Saxon, Andrew; Zhang, Ke; Zhu, Daocheng (Regents of the University of California, USA). PCT Int. Appl. WO 2002088317 A2 20021107, 116 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US13527 20020501. PRIORITY: US 2001-2001/847208 20010501; US 2001-2001/439 20011024.

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=> s l9 and IgG4
L18 3 L9 AND IGG4

=> dup remove l18
PROCESSING COMPLETED FOR L18
L19 3 DUP REMOVE L18 (0 DUPLICATES REMOVED)

=> d l19 1-3 cbib abs

L19 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
2004:292071 Document No. 140:320040 36Fusion proteins comprising CD1d complex, α2 microglobulin and antibody or fragment for targeting therapy of tumor, autoimmune disease, inflammation and infection. Robert, Bruno; Donda, Alena; Cesson, Valerie; Mach, Jean-Pierre; Zauderer, Maurice (Vaccinex, Inc., USA). PCT Int. Appl. WO 2004029206 A2 20040408, 152 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US30238 20030926. PRIORITY: EP 2002-405838 20020927.

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L19 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
2003:260853 Document No. 138:285999 Chimeric proteins comprising ITIM motif, antigen and FcεR binding peptide for treating immune diseases. Saxon, Andrew (USA). U.S. Pat. Appl. Publ. US 2003064063 A1 20030403, 51 pp., Cont.-in-part of U.S. Ser. No. 847,208. (English). CODEN: USXXCO. APPLICATION: US 2001-439 20011024. PRIORITY: US 2001-2001/847208 20010501.

AB The invention concerns bifunctional **fusion** mols., and novel, safer and more efficacious methods for the treatment of immune disorders resulting from excessive or unwanted immune responses. The invention provides methods for the suppression of type I hypersensitive (i.e., IgE-mediated) allergic conditions, methods for the prevention of anaphylactic responses that occur as a result of traditional peptide immunotherapies for allergic and autoimmune disorders, and provides novel methods for the treatment of autoimmune conditions, where the methods have reduced risk of triggering an anaphylactic response. The invention provides novel therapeutic approaches for the treatment of allergic responses, including the prevention of anaphylactic response that can occur from environmental allergen exposure. The invention also provides methods for the treatment of autoimmune disorders such as multiple sclerosis, autoimmune type I diabetes mellitus, and rheumatoid arthritis. The invention also provides methods for preventing anaphylactic response during traditional antigen therapies.

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=> s saxon a?/au
L20       1399 SAXON A?/AU

=> s l20 and fusion
L21         50 L20 AND FUSION

=> s l1 and IgG
L22      10673 L1 AND IGG

=> s l21 and Fc
L23         34 L21 AND FC

=> dup remove l23
PROCESSING COMPLETED FOR L23
L24          11 DUP REMOVE L23 (23 DUPLICATES REMOVED)

=> d l24 1-11 cbib abs

L24  ANSWER 1 OF 11  EMBASE  COPYRIGHT (c) 2006 Elsevier B.V. All rights
     reserved on STN                                    DUPLICATE 1
2005187007  EMBASE  A chimeric human-cat fusion protein blocks
     cat-induced allergy. Zhu D.; Kepley C.L.; Zhang K.; Terada T.; Yamada T.;
     Saxon A.. D. Zhu, Hart and Louise Lyon Laboratory, Department of
     Medicine, UCLA School of Medicine, 10833 Le Conte Avenue, Los Angeles, CA
     90095-1680, United States. dczhu@ucla.edu. Nature Medicine  Vol. 11, No.
     4, pp. 446-449  2005.
     Refs: 28.
     ISSN: 1078-8956. CODEN: NAMEFI
     Pub. Country: United Kingdom. Language: English. Summary Language:
     English.
ED   Entered STN: 20050602
AB   Animal allergens are an important cause of asthma and allergic rhinitis.
     We designed and tested a chimeric human-cat fusion protein
     composed of a truncated human IgG Fc.gamma.1 and the major cat
     allergen Fel d1, as a proof of concept for a new approach to allergy
     immunotherapy. This Fc.gamma.-Fel d1 protein induced
     dose-dependent inhibition of Fel d1-driven IgE-mediated histamine release
     from cat-allergic donors' basophils and sensitized human cord
     blood-derived mast cells. Such inhibition was associated with altered Syk
     and ERK signaling. The Fc.gamma.-Fel d1 protein also blocked in
     vivo reactivity in Fc.epsilon.RIα transgenic mice
     passively sensitized with human IgE antibody to cat and in Balb/c mice
     actively sensitized against Fel d1. The Fc.gamma.-Fel d1
     protein alone did not induce mediator release. Chimeric human Fc
     γ-allergen fusion proteins may provide a new therapeutic
     platform for the immune-based therapy of allergic disease.

L24  ANSWER 2 OF 11  EMBASE  COPYRIGHT (c) 2006 Elsevier B.V. All rights
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reserved on STN DUPLICATE 2
2004357862 EMBASE Co-aggregation of **Fc**.gamma.RII with **Fc** εRI on human mast cells inhibits antigen-induced secretion and involves SHIP-Grb2-Dok complexes. Kepley C.L.; Taghavi S.; Mackay G.; Zhu D.; Morel P.A.; Zhang K.; Ryan J.J.; Satin L.S.; Zhang M.; Pandolfi P.P.; **Saxon A.**. C.L. Kepley, Dept. of Internal Medicine, Div. of Rheumatol., Allerg./Immunol., MCV Station, P. O. Box 263, Richmond, VA 23298, United States. clkepley@mail1.vcu.edu. Journal of Biological Chemistry Vol. 279, No. 34, pp. 35139-35149 20 Aug 2004.
Refs: 64.
ISSN: 0021-9258. CODEN: JBCHA3
Pub. Country: United States. Language: English. Summary Language: English.
ED Entered STN: 20040916
AB Signaling through the high affinity IgE receptor **Fc**.epsilon.RI on human basophils and rodent mast cells is decreased by co-aggregating these receptors to the low affinity IgG receptor **Fc**.gamma.RII. We used a recently described **fusion** protein, GE2, which is composed of key portions of the human γ1 and the human ε heavy chains, to dissect the mechanisms that lead to human mast cell and basophil inhibition through co-aggregation of **Fc**.gamma.RII and **Fc**.epsilon.RI. Unstimulated human mast cells derived from umbilical cord blood express the immunoreceptor tyrosine-based inhibitory motif-containing receptor **Fc**.gamma.RII but not **Fc** γRI or **Fc**.gamma.RIII. Interaction of the mast cells with GE2 alone did not cause degranulation. Co-aggregating **Fc** εRI and **Fc**.gamma.RII with GE2 1) significantly inhibited IgE-mediated histamine release, cytokine production, and Ca(2+) mobilization, 2) reduced the antigen-induced morphological changes associated with mast cell degranulation, 3) reduced the tyrosine phosphorylation of several cellular substrates, and 4) increased the tyrosine phosphorylation of the adapter protein downstream of kinase 1 (p62(dok); Dok), growth factor receptor-bound protein 2 (Grb2), and SH2 domain containing inositol 5-phosphatase (SHIP). Tyrosine phosphorylation of Dok was associated with increased binding to Grb2. Surprisingly, in non-stimulated cells, there were complexes of phosphorylated SHIP-Grb2-Dok that were lost upon IgE receptor activation but retained under conditions of **Fc**.epsilon.-**Fc**.gamma. co-aggregation. Finally, studies using mast cells from Dok-1 knock-out mice showed that IgE alone triggers degranulation supporting an inhibitory role for Dok degranulation. Our results demonstrate how human **Fc** εRI-mediated responses can be inhibited by co-aggregation with **Fc**.gamma.RIIB and implicate Dok, SHIP, and Grb2 as key intermediates in regulating antigen-induced mediator release.

L24 ANSWER 3 OF 11 MEDLINE on STN DUPLICATE 3
2005032334. PubMed ID: 15640700. Genetically engineered negative signaling molecules in the immunomodulation of allergic diseases. **Saxon Andrew**; Zhu Daocheng; Zhang Ke; Allen Lisa Chan; Kepley Christopher L. (The Hart and Louise Lyon Laboratory, Division of Clinical Immunology/Allergy, Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA 90095-1680, USA.. asaxon@mednet.ucla.edu) . Current opinion in allergy and clinical immunology, (2004 Dec) Vol. 4, No. 6, pp. 563-8. Ref: 29. Journal code: 100936359. ISSN: 1528-4050. Pub. country: United States. Language: English.
AB PURPOSE OF REVIEW: This review summarizes current knowledge regarding the control of human mast cell and basophil signaling and recent developments using a new therapeutic platform consisting of a human bifunctional gamma and epsilon heavy chain (**Fc** gamma-**Fc** epsilon) protein to inhibit allergic reactivity. RECENT FINDINGS: Crosslinking of **Fc** gamma RIIb to **Fc** epsilon RI on human mast cells and basophils by a genetically engineered **Fc** gamma-**Fc** epsilon protein (GE2) leads to the inhibition of mediator release upon **Fc** epsilon RI challenge. GE2 protein was shown to inhibit cord blood-derived mast cell and peripheral blood basophil mediator release in

vitro in a dose-dependent fashion, including inhibition of human IgE reactivity to cat. IgE-driven mediator release from lung tissue was also inhibited by GE2. The mechanism of inhibition in mast cells included alterations in IgE-mediated Ca mobilization, spleen tyrosine kinase phosphorylation and the formation of downstream of kinase-growth factor receptor-bound protein 2-SH2 domain-containing inositol 5-phosphatase (dok-grb2-SHIP) complexes. Proallergic effects of Langerhan's like dendritic cells and B-cell IgE switching were also inhibited by GE2. In vivo, GE2 was shown to block passive cutaneous anaphylaxis driven by human IgE in mice expressing the human **Fc** epsilon RI and inhibit skin test reactivity to dust mite antigen in a dose-dependent manner in rhesus monkeys. SUMMARY: The balance between positive and negative signaling controls mast cell and basophil reactivity, which is critical in the expression of human allergic diseases. This approach using a human **Fc** gamma-**Fc** epsilon **fusion** protein to co-aggregate **Fc** epsilon RI with the **Fc** gamma RII holds promise as a new therapeutic platform for the immunomodulation of allergic diseases and potentially other mast cell/basophil-dependent disease states.

L24 ANSWER 4 OF 11 MEDLINE on STN DUPLICATE 4

2004433011. PubMed ID: 15316510. Inhibition of allergen-specific IgE reactivity by a human Ig Fcgamma-Fcepsilon bifunctional **fusion** protein. Zhang Ke; Kepley Christopher L; Terada Tetsuya; Zhu Daocheng; Perez Hector; **Saxon Andrew.** (Hart and Louis Lyon Laboratory, Division of Clinical Immunology and Allergy, Department of Medicine, University of California Los Angeles School of Medicine, CA 90095-1680, USA.) The Journal of allergy and clinical immunology, (2004 Aug) Vol. 114, No. 2, pp. 321-7. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: Coaggregating FcepsilonRI with FcgammaRII receptors holds great potential for treatment of IgE-mediated disease by inhibiting FcepsilonRI signaling. We have previously shown that an Fcgamma-Fcepsilon **fusion** protein, human IgG-IgE **Fc fusion** protein (GE2), could inhibit FcepsilonRI-mediated mediator releases in vitro and in vivo. OBJECTIVE: We sought to test whether GE2 was capable of blocking mediator release from FcepsilonRI cells sensitized with IgE in vivo or in vitro before exposure to GE2, a critical feature for GE2 to be clinically applicable. METHODS: GE2 was tested for its ability to inhibit Fel d 1-induced mediator release from human blood basophils from subjects with cat allergy, human lung-derived mast cells, human FcepsilonRIalpha transgenic mice sensitized with human cat allergic serum, and rhesus monkeys naturally allergic to the dust mite Dermatophagoides farinae. RESULTS: Basophils from subjects with cat allergy and lung mast cells degranulate when challenged with Fel d 1 and anti-IgE, respectively. GE2 itself did not induce mediator release but strongly blocked this Fel d 1- and anti-IgE-driven mediator release. GE2 was able to block Fel d 1-driven passive cutaneous anaphylaxis at skin sites sensitized with human serum from subjects with cat allergy in human FcepsilonRIalpha transgenic mice, but by itself, GE2 did not induce a passive cutaneous anaphylaxis reaction. Finally, GE2 markedly inhibited skin test reactivity to D farinae in monkeys naturally allergic to this allergen, with complete inhibition being observed at 125 ng. CONCLUSION: GE2 is able to successfully compete for FcepsilonRs and FcgammaRs on cells presensitized in vitro and in vivo and lead to inhibition of IgE-mediated reactivity through coaggregation of FcepsilonRI with FcgammaRII.

L24 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

2003:260853 Document No. 138:285999 Chimeric proteins comprising ITIM motif, antigen and **Fc**.epsilon.R binding peptide for treating immune diseases. **Saxon, Andrew** (USA). U.S. Pat. Appl. Publ. US 2003064063 A1 20030403, 51 pp., Cont.-in-part of U.S. Ser. No. 847,208. (English). CODEN: USXXCO. APPLICATION: US 2001-439 20011024. PRIORITY: US 2001-2001/847208 20010501.

AB The invention concerns bifunctional **fusion** mols., and novel,

safer and more efficacious methods for the treatment of immune disorders resulting from excessive or unwanted immune responses. The invention provides methods for the suppression of type I hypersensitive (i.e., IgE-mediated) allergic conditions, methods for the prevention of anaphylactic responses that occur as a result of traditional peptide immunotherapies for allergic and autoimmune disorders, and provides novel methods for the treatment of autoimmune conditions, where the methods have reduced risk of triggering an anaphylactic response. The invention provides novel therapeutic approaches for the treatment of allergic responses, including the prevention of anaphylactic response that can occur from environmental allergen exposure. The invention also provides methods for the treatment of autoimmune disorders such as multiple sclerosis, autoimmune type I diabetes mellitus, and rheumatoid arthritis. The invention also provides methods for preventing anaphylactic response during traditional antigen therapies.

L24 ANSWER 6 OF 11 MEDLINE on STN DUPLICATE 5

2003414071. PubMed ID: 12801927. Inhibition of interleukin-4-induced class switch recombination by a human immunoglobulin **Fc** gamma-**Fc** epsilon chimeric protein. Yamada Takechiyo; Zhu Daocheng; Zhang Ke; **Saxon Andrew.** (Hart and Louis Laboratory, Division of Clinical Immunology, Department of Medicine, UCLA School of Medicine, California 90095-1680, USA.. ymdtkcy@fmsrsa.fukui-med.ac.jp) . The Journal of biological chemistry, (2003 Aug 29) Vol. 278, No. 35, pp. 32818-24. Electronic Publication: 2003-06-11. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Immunoglobulin E (IgE) is important in mediating human allergic diseases. We tested the hypothesis that a human Ig **Fc** gamma-**Fc** epsilon bifunctional chimeric protein, GE2, would inhibit IgE class switch recombination (CSR) by co-aggregating B-cell CD32 and CD23. Indeed, GE2 directly inhibited epsilon germ-line transcription, subsequent CSR to epsilon and IgE protein production. This CSR inhibition was dependent on CD23 binding and the phosphorylation of extracellular signal-related kinase (ERK), and it was mediated via suppression of interleukin-4-induced STAT6 phosphorylation. Treatment with PD98059, a specific inhibitor of mitogen-activated protein kinase kinase 1 (MAPKK1 (MEK1)) and MEK2 reversed the ability of GE2 to decrease CSR and STAT6 phosphorylation. GE2 stimulation induced ERK phosphorylation, whereas it did not alter the phosphorylation of c-Jun N-terminal kinase or p38 MAPK. The ability of GE2 to block human isotype switching to epsilon, in addition to its already demonstrated ability to inhibit mast cell and basophil function, suggests that it will provide an important novel benefit in the treatment of IgE-mediated diseases.

L24 ANSWER 7 OF 11 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 6

2003323238 EMBASE **Fc**.epsilon.RI-**Fc**.gamma.RII coaggregation inhibits IL-16 production from human langerhans-like dendritic cells. Kepley C.L.; Zhang K.; Zhu D.; **Saxon A.**. C.L. Kepley, Department of Internal Medicine, Div. Rheumatolgy, Allerg./Immunol., P.O. Box 263 MCV Station, Richmond, VA 23298, United States. clkepley@mail1.veu.edu. Clinical Immunology Vol. 108, No. 2, pp. 89-94 1 Aug 2003.
Refs: 28.
ISSN: 1521-6616. CODEN: CLIIFY
Pub. Country: United States. Language: English. Summary Language: English.

ED Entered STN: 20030828

AB Langerhans-like dendritic cells (LLDC) express the high-affinity IgE receptor **Fc**.epsilon.RI form that lacks the β-chain, and may play an important role in allergic inflammation via production of IL-16. Secretion of mediators by human mast cells and basophils is mediated through **Fc**.epsilon.RI and is decreased by coaggregating these receptors to the low-affinity IgG receptor, **Fc**.gamma.RII. We used a recently described human Ig **fusion** protein (GE2), which is composed of key portions of the human γ1 and the human ε

heavy chains, to investigate its ability to inhibit IL-16 production from **Fc**.epsilon.RI-positive Langerhans-like dendritic cells through coaggregation of **Fc**.gamma.RII and **Fc**.epsilon.RI. Unstimulated LLDC-derived from CD14-positive monocytes from atopic donors were shown to express **Fc**.gamma.RII, an ITIM-containing receptor, but not **Fc**.epsilon.RI or **Fc**.gamma.RIII which are activating (ITAM) receptors. When passively sensitized with antigen-specific, human IgE and then challenged with antigen, LLDC were stimulated to produce IL-16. However, when **Fc**.epsilon.RI and **Fc**.gamma.RII were coaggregated with GE2, IL-16 production was significantly inhibited. Exposure of LLDCs to GE2 alone did not induce IL-16 production. Our results further extend our studies demonstrating the ability of GE2 to inhibit **Fc**.epsilon.RI-mediated responses through coaggregation with **Fc**.gamma.RIIB and at the same time show that human LDCC can be modulated in a fashion similar to mast cells and basophils. .COPYRGT. 2003 Elsevier Inc. All rights reserved.

L24 ANSWER 8 OF 11 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2004:72749 Document No.: PREV200400071901. SHIP-Grb2-Dok complexes prevent **Fc**(epsilon)RI-mediated human mast cell activation and regulate **Fc**(gamma)RII-mediated inhibition. Kepley, Christopher Lynn [Reprint Author]; Mackay, Graham; Morel, Penelope A.; Zhu, Daocheng; Ke, Zhang; **Saxon, Andrew.** Internal Medicine, Medical College of Virginia, Virginia Commonwealth University, 1112 E Clay St, McGuire Hall Room 4-115B, Richmond, VA, 23298, USA. FASEB Journal, (April 14 2003) Vol. 17, No. 7, pp. C15. print.
Meeting Info.: 90th Anniversary Annual Meeting of the American Association of Immunologists. Denver, CO, USA. May 06-10, 2003. American Association of Immunologists.
ISSN: 0892-6638 (ISSN print). Language: English.

L24 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
2002:849789 Document No. 137:368556 Chimeric proteins comprising IgG inhibitory receptor-binding epitope and IgE receptor-binding epitope for treating allergies and other immune diseases. **Saxon, Andrew;** Zhang, Ke; Zhu, Daocheng (Regents of the University of California, USA). PCT Int. Appl. WO 2002088317 A2 20021107, 116 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US13527 20020501. PRIORITY: US 2001-2001/847208 20010501; US 2001-2001/439 20011024.
AB The invention concerns bifunctional **fusion** mols., and novel, safer and more efficacious methods for the treatment of immune disorders resulting from excessive or unwanted immune responses. The invention provides methods for the suppression of type I hypersensitive (i.e., IgE-mediated) allergic conditions, methods for the prevention of anaphylactic responses that occur as a result of traditional peptide immunotherapies for allergic and autoimmune disorders, and provides novel methods for the treatment of autoimmune conditions, where the methods have reduced risk of triggering an anaphylactic response. The invention provides novel therapeutic approaches for the treatment of allergic responses, including the prevention of anaphylactic response that can occur from environmental allergen exposure. The invention also provides methods for the treatment of autoimmune disorders such as multiple sclerosis, autoimmune type I diabetes mellitus, and rheumatoid arthritis. The invention also provides methods for preventing anaphylactic response during traditional antigen therapies.

L24 ANSWER 10 OF 11 MEDLINE on STN DUPLICATE 7

2002245565. PubMed ID: 11984598. A novel human immunoglobulin **Fc** gamma **Fc** epsilon bifunctional **fusion** protein inhibits **Fc** epsilon RI-mediated degranulation. Zhu Daocheng; Kepley Christopher L; Zhang Min; Zhang Ke; **Saxon Andrew.** (The Hart and Louise Lyon Laboratory, Division of Clinical Immunology/Allergy, Department of Medicine, University of California Los Angeles School of Medicine, Los Angeles, California, USA.) Nature medicine, (2002 May) Vol. 8, No. 5, pp. 518-21. Journal code: 9502015. ISSN: 1078-8956. Pub. country: United States. Language: English.

AB Human mast cells and basophils that express the high-affinity immunoglobulin E (IgE) receptor, **Fc** epsilon receptor 1 (**Fc** epsilon RI), have key roles in allergic diseases. **Fc** epsilon RI cross-linking stimulates the release of allergic mediators. Mast cells and basophils co-express **Fc** gamma RIIb, a low affinity receptor containing an immunoreceptor tyrosine-based inhibitory motif and whose co-aggregation with **Fc** epsilon RI can block **Fc** epsilon RI-mediated reactivity. Here we designed, expressed and tested the human basophil and mast-cell inhibitory function of a novel chimeric **fusion** protein, whose structure is gamma Hinge-CH gamma 2-CH gamma 3-15aa linker-CH epsilon 2-CH epsilon 3-CH epsilon 4. This **Fc** gamma **Fc** epsilon **fusion** protein was expressed as the predicted 140-kappa D dimer that reacted with anti-human epsilon- and gamma-chain specific antibodies. **Fc** gamma **Fc** epsilon bound to both human **Fc** epsilon RI and **Fc** gamma RII. It also showed dose- and time-dependent inhibition of antigen-driven IgE-mediated histamine release from fresh human basophils sensitized with IgE directed against NIP (4-hydroxy-3-iodo-5-nitrophenylacetyl). This was associated with altered Syk signaling. The **fusion** protein also showed increased inhibition of human anti-NP (4-hydroxy-3-nitrophenylacetyl) and anti-dansyl IgE-mediated passive cutaneous anaphylaxis in transgenic mice expressing human **Fc** epsilon RI alpha. Our results show that this chimeric protein is able to form complexes with both **Fc** epsilon RI and **Fc** gamma RII, and inhibit mast-cell and basophil function. This approach, using a **Fc** gamma **Fc** epsilon **fusion** protein to co-aggregate **Fc** epsilon RI with a receptor containing an immunoreceptor tyrosine-based inhibition motif, has therapeutic potential in IgE- and **Fc** epsilon RI-mediated diseases.

L24 ANSWER 11 OF 11 MEDLINE on STN DUPLICATE 8

94267214. PubMed ID: 7515920. CD58 (LFA-3) stimulation provides a signal for human isotype switching and IgE production distinct from CD40. Diaz-Sanchez D; Chegini S; Zhang K; **Saxon A.** (Hart and Louise Lyon Laboratory, Department of Medicine, UCLA School of Medicine 90024-1680.) Journal of immunology (Baltimore, Md. : 1950), (1994 Jul 1) Vol. 153, No. 1, pp. 10-20. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Induction of an IgE response involves several discrete steps: 1) induction of epsilon germ line transcription, 2) DNA recombination, and 3) mature RNA transcription/translation. Here we show that ligation of B cell CD58 by CD2, its natural ligand on T cells, or by mAb, provides a novel IL-4-dependent signal for the latter two steps. Highly purified human B cells were induced to produce IgE by costimulation with IL-4 and CD58 mAb. Although CD58 ligation alone was unable to induce epsilon germ-line transcription, in concert with IL-4-stimulated epsilon germ-line transcription it induced the appearance of productive epsilon transcripts and IgE production. The direct involvement of CD2 was demonstrated: B cells cultured with IL-4 plus murine T hybridoma cells transfected with human CD2 produced IgE. A CD40 **Fc fusion** protein had no effect on CD58-driven IgE production while inhibiting CD40-dependent responses. Furthermore, cells from patients with common variable immunodeficiency produced IgE in response to IL-4 plus CD40 mAb but not to IL-4 plus CD58 mAb. CD58-driven IgE synthesis was IFN-gamma independent and was not enhanced by exogenous IL-6. Functional differences between CD40 and CD58 IgE stimulation were demonstrated. Thus, the CD2:CD58

ligand/counterligand system provides an alternative pathway by which cell contact signaling may regulate IgE. Given the relative importance of CD2 triggering on mucosal T cells and the mucosal location of IgE production, this may be especially true on mucosal surfaces.

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